AUG 27 1928

VOLUME 15 NUMBER 2

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FEBRUARY, 1927

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, October 30, 1917, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on July 29, 1918.

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Archives of Dermatology and Syphilology

VOLUME 15 FEBRUARY, 1927 NUMBER 2

THE USE OF GOLD AND SODIUM THIOSULPHATE IN THE TREATMENT OF LUPUS ERYTHEMATOSUS

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PHILADELPHIA

The first use of gold in lupus erythematosus was doubtless based on the assumption that this disease was of tuberculous origin, for gold was employed in tuberculosis according to White [1] as far back as 1810 by Chrestien. Robert Koch, however, in 1890, gave the impetus to the use of gold after he had demonstrated its effect on the tubercle bacillus in vitro.

Bruck and Glück [2] were the first in recent years to institute treatment with gold in tuberculosis. These investigators tried the effect of potassium gold cyanide injections intravenously in lupus vulgaris. They state that "there is no doubt that by intravenous injection of potassium-gold cyanide, without local treatment, a striking improvement in lupus lesions is produced." This is justified by the photographs published by them which leave no doubt as to the demonstrably favorable effects on the cutaneous lesions. No complete cures were effected however. The influence was increased when tuberculin injections were associated with the gold treatment.

Oberstadt [3] likewise obtained good results in cutaneous lesions, but no complete or perfect cures.

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* From the Research Institute of Cutaneous Medicine.

1. White: Am. Med. Surg. Bull. **7**:388, 1894.

2. Bruck and Glück: München. med. Wchnschr. **60**:57, 1913.

3. Oberstadt: Internat. Centralbl. f. d. ges. Tuberk.-Forsch. **40**:1, 1917; abstr., Am. Rev. Tuberc. **1**:737, 1918.

Junker [4] reported good results from the use of salts of gold in pulmonary and skin tuberculosis in human subjects. Poor and Geber [5] also obtained good results in the treatment of tuberculosis of the skin with potassium gold cyanide.

Spiess and Feldt in a series of papers published separately and in collaboration reported between 1912 and 1916 on the use of various gold combinations in tuberculosis. Feldt [6] found that tubercle bacilli were restrained in culture by colloidal gold in dilutions of 1 : 1,000,000 and by potassium cyanide in dilutions of 1 : 1,000. He regarded potassium gold cyanide as too toxic a preparation for human use. As cantharidin had been found earlier to produce focal reactions in tuberculous tissue, this substance was condensed with ethylenediamin and combined with cyanide of gold. The toxicity of this monocantharidyl-ethylenediamin-aurous cyanide was much less than the cyanide of gold and potassium. Spiess and Feldt claimed that the favorable effects were due in part to the influence of the compound on the tubercle bacillus and in part to the stimulation of the defensive mechanism of the body.

In 1917 Feldt [7] elaborated another gold compound, the *4*-amino-*2*-aurothiophenol carbonic acid, to which was given the name "Krysolgan." This possesses a tuberculin-like effect on tuberculous tissues, and is said to restrain growths of tubercle bacilli in a concentration of 1 : 1,000,000. During the last seven years it has been extensively employed in Germany in cutaneous and other forms of tuberculosis. A curative effect on tuberculosis in rabbits could not be demonstrated by Gorke or Töppich [8] with Krysolgan, and Kolle and Schlossberger [9] were able to show only some retardation of death. Krysolgan has been employed considerably in lupus erythematosus, a disease which many authors consider to be intimately related to, if not caused by, tuberculosis.

LUPUS ERYTHEMATOSUS

Apparently the first clinician to use gold in the treatment of lupus erythematosus was Ruete,[10] who employed gold potassium cyanide. One case of discoid lupus erythematosus was uninfluenced by three injections of this drug, 0.09 Gm. being given in all. In a second case of acute

4. Junker: München. med. Wchnschr. **60**:1376, 1913; Beitr. z. Klin. d. Tuberk. **7**:421, 1914.

5. Poor and Geber: Deutsche med. Wchnschr. **39**:1303, 1913.

6. Feldt: Deutsche med. Wchnschr. **40**:579, 1914; Berl. klin. Wchnschr. **82**:365, 1915; München. med. Wchnschr. **61**:842 and 1455, 1914.

7. Feldt: Berl. klin. Wchnschr. **54**:1111, 1917; München. med Wchnschr. **67**:1500, 1920; Therap. Monatsh. **32**:241, 1918.

8. Gorke and Töppich: Beitr. z. Klin. d. Tuberk. **53**:132, 1922.

9. Kolle and Schlossberger: Zentralbl. f. d. ges. ToKunde **19**:341, 1923.

10. Ruete: Deutsche med. Wchnschr. 1913, p. 1727.

lupus erythematosus there was complete healing after seven injections of the same drug, a total of 0.23 Gm. being given.

In 1921, Kohrs [11] reported the complete disappearance of lupus erythematosus following the use of Krysolgan. While the injections were being given the patient developed stomatitis.

In the same year Sainz de Aja reported improvement in a case of lupus erythematosus of the face from the use of gold potassium cyanide. After eight injections his patient developed a fever, a papulovesicular exanthem and edema of the face.

Brock [12] treated a patient with Krysolgan, and central healing of the patch resulted.

Martenstein [13] was the first to have a large experience with this therapy. He treated forty-two patients, with clinical cure in twenty-eight (66.5 per cent), and improvement in six (14.5 per cent); four were unimproved, and in four the condition was aggravated. The last named patients improved for a time under gold therapy, but with increase of the dose became worse; this was attributed to overdosage. Krysolgan was used in all of these cases. In five cases there was a tendency to relapse some time later. Two injections were given weekly, the dose being gradually increased from 0.05 to 0.2 Gm. Twenty of the patients developed an exanthem from the injections. Stomatitis was not uncommon. Martenstein observed also in some instances fever, edema, urticaria and enteritis.

Fried [14] reported on the treatment with Krysolgan in fifteen cases of lupus erythematosus at the 1922 meeting of the Wiener Dermatologische Gesellschaft. In three of these cases there was clinical cure, in eight considerable improvement, in two slight improvement and in two no change. The slightly erythematous hyperkeratotic type reacted the most favorably to treatment.

In 1923 Ullmann [15] reported at the Wiener Dermatologische Gesellschaft on treatment with Krysolgan in three cases. Clinical cure was obtained in five or six weeks, injections being given weekly and never in a dosage over 0.1 Gm. He later [16] reports the results of the use of this preparation in eight cases of lupus erythematosus, in all of which it was successful. In a few of the cases tuberculin was also administered, and in some an organic iodine compound. In discussing this paper before the Vienna Medical Society, Nobel was unable to substantiate the claims

11. Kohrs: Dermat. Wchnschr., 1921, p. 181.
12. Brock: Abstr., Zentralbl. f. Haut. u. geschl. Krankh. **4**:442, 1921.
13. Martenstein: Klin. Wchnschr. **1**:2235, 1922.
14. Fried, at the meeting of the Wiener Dermatologische Gesellschaft, 1922.
15. Ullmann, at the meeting of the Wiener Dermatologische Gesellschaft, 1923.
16. Ullmann: Wien. klin. Wchnschr. **23**:579, 1924.

of Ullmann. Volk agreed with Ullmann as to its beneficial effects. He had treated some twenty-seven patients and had rapidly favorable results, particularly in the chronic hyperkeratotic forms. Gruss of Finger's Clinic stated that he had seen favorable results only in the early stages of lupus erythematosus, but that in using it in combination with an organic iodine compound, he had secured cures in the cases with marked infiltration. In lupus vulgaris, thus far, Krysolgan seems to have achieved but little. Rickmann [17] refers to a new gold compound more recently elaborated in Germany under the name of "Triphal." He states that the effect of this drug given intravenously in tuberculosis of the larynx and in combination with other methods can no longer be contested. Definite judgment is not yet at hand with regard to its value in tuberculosis of the skin. From a chemical standpoint this preparation differs from Krysolgan through its greater stability. Krysolgan degenerates relatively easily, whereas the separation of gold from Triphal does not occur so rapidly in the presence of slight moisture. From a pharmacologic standpoint, the latter is said to be only half as poisonous as the former in warm-blooded animals.

Westphalen [18] treated nine patients with Krysolgan. In four cases there was complete healing, in two partial healing, in two slight improvement, and in one no change. The dose was gradually increased from 0.025 to 0.1 Gm. Improvement usually took place by the time 0.3 Gm. had been given, and in no case was a total of 1.8 Gm. exceeded.

Deaths have been observed after the use of gold. Stein observed deaths after three injections, and Bruhns a death forty-four hours after an injection of 0.001 of Krysolgan. Tryb observed the dissemination of a case of lupus erythematosus after an injection of Krysolgan.

In 1924, Møllgard of Copenhagen published a book on "The Chemotherapy of Tuberculosis," in which he elaborated the virtues of a perfected compound of gold with thiosulphuric acid, which was produced first by Fordos and Gelis [19] in 1845. A pure body with constant chemical and physical properties can be made by way of synthesis indicated by Fordos and Gelis, but it is necessary to recrystallize it four or five times from a mixture of alcohol and water. The yields are poor and the final product contains only from 10 to 15 per cent of the gold orginally employed. By Møllgard's [20] method the product contains from 90 to 95 per cent of the gold employed after one crystallization. This product, to which the name "sanocrysin" (sodium and gold thiosulphate) was given, is snow white, occurs in long needles and is easily soluble in

17. Rickmann: München. med. Wchnschr **71**:1609 (Nov. 14) 1924.
18. Von Westphalen, F.: Deutsche med. Wchnschr. **49**:1520 (Dec.) 1923.
19. Fordos and Gelis: Ann. Chem. Phys. **13**:394, 1845.
20. Møllgard: The Chemotherapy of Tuberculosis, Copenhagen, Busck, 1924.

water, with an almost neutral reaction. It is slowly decomposible, and does not precipitate serum even at 40 C. in twenty-four hours. It is not supposed to form gold ions in the body. It retards the growth of the tubercle bacillus in concentration of 1:1,000,000, and prevents it in 1:100,000.

The minimal lethal dose of this drug in guinea-pigs is 30 mg. per kilogram given intraperitoneally, and in rabbits, 40 mg. per kilogram, intravenously. Calves tolerate 60 mg. per kilogram intravenously. Møllgard makes the following experimental claims for the drug: 1. It prevents growth of tubercle bacilli in culture. 2. It makes the fatty system which protects the tubercle bacilli penetrable to hydrogen and metal ions. 3. It prevents infected guinea-pigs from getting generalized tuberculosis. 4. Injected into the tuberculous organism it produces all the reactions which are expected to follow the injection of a substance having a bactericidal influence on tubercle bacilli. 5. Injected into non-tuberculous organisms in therapeutic doses it produces no reactions.

It should be here remarked that in the guinea-pigs in which subcutaneous inoculations were performed, injections of from 10 to 20 mg. were immediately made into the infected area.

Schamberg, Harkins and Brown [21] studied the effect of various gold compounds on experimental tuberculosis of the skin in rabbits. They observed a demonstrable effect on experimentally induced cutaneous lesions, and a prolongation of life beyond the average of the infected controls.

GOLD AND SODIUM THIOSULPHATE IN LUPUS ERYTHEMATOSUS

To the best of our knowledge sodium and gold-thiosulphate has not hitherto been used in lupus erythematosus. The results with this compound in lupus erythematosus in our own cases and in the patients of other dermatologists to whom we have furnished the drug have been so striking that we have come to regard gold as having almost a specific effect in this disease. We have records of its use in twenty-five patients with results as follows: The eruption has disappeared in five cases. It has almost disappeared in six cases. Improvement has resulted in twelve cases (a number of the patients are still under treatment). In one patient there was no improvement. One patient died. For a disease which in the past has been so obstinate and intractable as to be regarded as the bete noir of dermatologists, these results, to say the least, are noteworthy.

In order to present a more concrete idea of the progress made in individual cases, we will quote from the letters of colleagues as well as give our own experience.

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21. Schamberg, J. F.; Harkins, M. J., and Brown, H.: Gold Compounds in Treatment of Experimental Tuberculosis of Skin in Animals, Arch. Dermat. & Syph. **13**:43-54 (Jan.) 1926.

REPORT OF AUTHOR'S CASES

CASE 1.—J. E., aged 45, referred by Dr. J. Edgar Fisher of Cleveland, presented an extensive inflammatory eruption of two years' duration, consisting of numerous patches covering the entire face. The nose was particularly involved. His general health was good. The patient was given 100 mg. of gold and sodium thiosulphate intravenously on July 10, 1926. He was then sent back to Dr. Fisher, who gave him a second injection. Some hours later the patient developed chills, a temperature of 101 F. and a pulse rate of 100. The patient was confined to his bed for one week feeling tired and having no appetite. He had occipital headaches and chills twice daily. Under the date of Aug. 23, 1926, Dr. Fisher wrote: "The condition on his face has cleared up entirely. The most wonderful improvement I have ever seen." The patient's face now looks normal. On Sept. 29, 1926, Dr. Fisher wrote: "The patient is entirely free of his lupus erythematous."

CASE 2.—J. U., a man, aged 58, consulted us on account of a well marked lupus erythematosus, inflammatory patches covering the greater part of each side of the face, of 5 years' duration. He had received applications of carbon dioxide snow to the right cheek and, as a result, had a reddened scar approximately 2 by 4 cm. He received two injections of gold and sodium arsphenamine at weekly intervals, and in two weeks 50 per cent of the eruption had disappeared. He received three more injections of the gold arsphenamine with a disappearance of all lesions except the scar, which retained an angry appearance.

CASE 3.—Mrs. R. D., aged 38, presented a lupus erythematosus of one year's duration. The upper two thirds of the nose was covered with inflammatory hyperkeratotic crusted lesions. There was a patch about 2 cm. in diameter on the left cheek and a similar one on the chest. On March 12, 1926, she received an injection of 100 mg. of gold and sodium thiosulphate. At four day intervals four more doses were given, the last one being increased to 200 mg. After this injection the patient complained of feeling poorly, and in a few hours developed fever and later a swelling of the glands of the neck. Three days later the tonsils, which were diseased, were removed, following which she developed a lichenoid and eczematoid eruption over the neck, extremities and hands, a condition almost approaching an exfoliative dermatitis. Injections of sodium thiosulphate were then given, and in two weeks this eruption had disappeared, as well as the lupus erythematosus, with the exception of a residual hyperkeratosis of the nose without inflammation. The patient is still being treated.

CASE 4.—Mr. W. McC., aged 33, presented a lupus erythematosus of 2 years' duration. The entire nose was the seat of a crusted and hyperkeratotic infiltrated patch. Both ears showed similar lesions, and there was a discoid patch over the right malar eminence. Gold and sodium thiosulphate, 100 mg., was administered intravenously on April 29, 1926, and the patient was given pills containing 1/15 grain (0.004 Gm.) of gold chloride to take by mouth three times a day. Five more injections of 150 mg. each of gold and sodium thiosulphate were given at weekly intervals following which the lesions completely disappeared. At present there is no evidence of any tendency to recurrence.

CASE 5.—Mr. S. S., aged 51, presented a lupus erythematosus of three years' duration. The entire cheeks were covered with discoid markedly inflammatory patches. The patient stated that he was so embarrassed by the appearance of his face that he was loath to attend to his business as a salesman. On May 5, 1926, he was given an injection of 100 mg. of gold and sodium thiosulphate and the gold chloride by mouth, 1/15 grain (0.004 Gm.) three times a day. He was given three or four additional ampules, with instructions to his physician as to their administration. When last seen by us on October 8, he was virtually free from

Fig. 1 (case 6).—Severe eruption of eleven years' duration; had been treated by every conceivable method without result.

Fig. 2 (case 6).—Eruption has almost disappeared after about sixty injections of various gold compounds; some scarring and telangiectasis due to maladroit roentgen-ray treatment.

all lesions, only a slight erythema of the face persisting. In all this patient received not more than 700 or 800 mg. of the gold and sodium thiosulphate.

CASE 6.—Mrs. P., aged 28, presented an extensive lupus erythematosus of eleven years' duration.[22] The face was almost entirely covered, the eruption extending across the nose and involving the greater part of each cheek and the upper lip. There was a considerable redness, which was markedly accentuated over the upper lip, upper part of the cheeks and nose as a result of deep telangiectases, due to previous maladroit treatment with the roentgen ray. The ears, neck, chest and arms were also the seat of circumscribed scaly inflammatory patches. The face also presented a considerable area of cicatricial atrophy. This case was one of unusual severity and extent for the chronic type as seen in figure 1.

Treatment was instituted with "Aurophos" on Sept. 28, 1925, 0.0025 Gm. being given for an initial dose. Injections were given twice weekly until Feb. 25, 1926, the dose being gradually increased to 0.05 Gm. Improvement was noticed three weeks after the institution of the gold therapy and was marked by the middle of November, when the patient was presented at the annual meeting of the Atlantic Dermatological Conference in Philadelphia. February 25, gold and sodium thiosulphate was substituted, injections being given twice weekly (each dose 100 mg.) up to the present, with the exception of five weeks, when the number of injections was limited to one a week. In all this patient has had more than one hundred injections without reaction.

The patches which disappeared the most rapidly were those of most recent origin, which had received no roentgen-ray therapy. It is unfortunate that the roentgen ray was ever used in this case, for otherwise the eruption would probably have disappeared completely. It has proved necessary to apply carbon dioxide snow to the telangiectases involving the upper cheeks and the upper lip.

CASE 7.—L. D., aged 20, had a rather diffuse type of lupus erythematosus for four years, with periods of improvement. On Jan. 9, 1926, she presented patches on the nose, cheeks and chin. On a previous occasion there were also patches on the chest and arms. She had been operated on for an abscess of the leg a year before. She received an injection of Aurophos, a German gold compound. After three or four injections, the face looked rather worse. On January 23 there was considerable reaction on the face. Two long linear ulcerations, presenting a tuberculous appearance, showed themselves along the incision scar on the back of the leg. The face became worse gradually, and an inflammatory eruption appeared on the chest. The patient developed fever and was removed to the hospital. At the end of thirty-seven days, the patient became comatose and died. Permission for an autopsy examination was not obtained.

CASE 8.—Mrs. H. G., aged 44, presented a lupus erythematosus of three (?) years' duration. Almost the entire face was the seat of a purplish or bluish red eruption, covered with adherent scales. The patches were also present on the ears, the chest, the backs of the hands and the legs. Over the face there was a considerable degree of scarring. In February, 1926, an injection of gold chloride was given intravenously, following which the patient developed a severe urticaria. No further treatment was given until August 12, when 5 cc. of a 2 per cent colloidal suspension of gold chloride was injected intravenously. The same dose was injected at intervals of a week for four successive times. Following the fourth injection the patient again had a slight reaction and although there was marked improvement at this time, gold thiosulphate was substituted for the col-

22. She stated that if she could not be helped she would commit suicide.

Fig. 3 (case 8).—Lupus erythematosus of three (?) years' duration; bluish red eruption; tendency to disseminate type.

Fig. 4 (case 8).—Eruption has virtually disappeared after short course of gold treatment.

loidal gold solution. To date the patient has received six injections of 100 mg. each of gold thiosulphate in solution and is almost free from the eruption. In fact, at present it would be impossible to make a diagnosis.

Case 9.—Mr. R. B., aged 39, first developed the eruption on his face when he was a boy. It gradually spread until when first seen in 1925 the patient presented a reddish, almost purplish, telangiectatic eruption over the greater part of the face. The eruption had a glazed appearance; there was some scar formation. The patient gave the history of having had roentgen-ray treatment in 1910, having received two treatments a week for about three months. Injections of gold arsphenamine were first given early in 1925. He received five injections at

Fig. 5 (case 9).—Long standing case; eruption of twenty-five years' duration; patient received considerable roentgen-ray treatment some years before.

intervals of from three to four weeks without improvement. He was next given injections of the colloidal gold, and in December, 1925, the condition was markedly improved, the injections having been given at intervals of from three to four weeks from May on. In March, 1926, injections of gold thiosulphate were started, and he received 100 mg. at intervals of from two to three weeks, with a great degree of improvement. By the end of April 90 per cent of the eruption had disappeared. Improvement has continued until at present little of the lupus erythematosus remains.

OTHER CASES

Case 10.—A man, aged 29, referred to us in July, 1925, by Dr. C. L. Baskin of Akron, Ohio, presented extensive discoid patches on the face, which had

developed while he was in the army in 1918. The diagnosis of lupus erythematosus was made by Dr. Baskin. One hundred milligrams of gold arsphenamine was administered. Six more injections were given by Dr. Baskin. He was seen by us again in July, 1926, at which time there was a vast improvement in the eruption. Gold and sodium thiosulphate was then advised. Dr. Baskin wrote on October 12: "Patient was unable to earn a livehood and was given one-half total disability by the Veterans' Bureau. Now he is a salesman at a high salary; the scars are hardly noticeable. No activity for the past 20 months."

CASE 11.—A man, aged 41, according to notes supplied by Dr. Baskin, showed lupus erythematosus in patches confined to one ear and one side of the face. There were about five or six active lesions, roughly 2 by 2 cm. in diameter. There were several old scars. The patient received three injections of gold and sodium thiosulphate and was much improved. He did not return for further treatments.

Fig. 6 (case 9).—Eruption has almost disappeared under gold treatment.

CASE 12.—A patient of Dr. George M. MacKee, New York, aged 45, presented a discoid type of lupus erythematosus of the face, ears and neck, of ten years' duration. There were eight lesions, varying in size from 2 to 5 cm. The condition did not improve until eighteen injections of gold and sodium thiosulphate were given in the course of nine weeks. "Then the lesions completely disappeared within 2 to 3 weeks." Eighteen more injections were given, and the treatment was then discontinued. He was free from the eruption for three months. At present there is a slight recurrence and treatment has been resumed.

CASE 13.—A woman, aged 30, also a patient of Dr. MacKee, presented a severe example of the disseminate type of the disease of fifteen years' duration. It was universal on the scalp and face and there were scattered areas on the trunk and arms. Intravenous injections of 100 mg. of gold and sodium thiosulphate were given twice a week. After twenty injections there was a violent exacerbation or flare-up of the entire eruption, with chills and fever. The patient was confined to

his bed for a couple of weeks. "The generalized eruption may have been toxic or may have been a manifestation of lupus." In a month the exacerbation subsided and now the condition is slightly improved.

CASE 14.—A woman, aged 35, a patient of Dr. MacKee, "presented a severe disseminate type of the disease, mostly on the face and ears, but with a few lesions also on the scalp and the body. There was no improvement after twelve injections. Then the eruption became inflammatory and there was a more or less generalized toxic eruption, or perhaps an outbreak of lupus erythematosus, which persisted for from two to three weeks. The patient was quite ill and remained in bed. This was about three months ago. I have not seen the patient since. It is said that she is a little better than she was before the reaction."

CASES 15, 16 and 17.—Dr. A. Schuyler Clark, New York, treated three patients with a colloidal gold compound. The three cases were pronounced; two were of the discoid type and one, disseminated. "One discoid lupus erythematosus of the nose and lips is well." "Mrs. X. with the disseminated type is distinctly improved, the lesions being much thinner and fading, and the other discoid case is distinctly improved. All three cases had quite marked protein reactions when the dose reached 5 cc. . . . There is no question about the result of the gold protein in these cases of lupus erythematosus. . . . This is the first line of treatment that I have ever seen really influence lupus erythematosus."

CASE 18.—Dr. Paul E. Bechet, New York, saw an extensive case of lupus erythematosus disseminata. The face, chest and arms were entirely covered with the eruption. The general health of the patient was poor. Roentgenograms showed bilateral peribronchial thickening. A cough was present and there was rapid loss of weight. From 5 to 10 cc. of colloidal gold was injected intravenously twice a week with truly phenomenal results. After about three months the eruption had entirely disappeared, except for one or two small discoid patches on the neck. The patient has regained his weight and seems entirely well. There was a marked reaction after most of the injections.

CASE 19.—Dr. Bechet saw another case of lupus erythematosus of the discoid type of long standing. The eruption covered the entire face, ears and neck, and it was complicated by severe radio-dermatitis. The condition in this patient has improved; the lesions are less red and congested and there seems to be an increase in the areas of healthy skin.

CASE 20.—Dr. A. Segal, Brooklyn, saw a case of acute lupus erythematosus of the face, neck and back of the hand. It was also seen by Dr. Fred Wise, who stated that "the prognosis in a case of this kind is poor." The patient received ten injections of gold and sodium thiosulphate over a period of five weeks. Dr. Wise saw the patient again and wrote "the results of the injections in the case of Mr. L. are simply phenomenal. I have never seen a case respond like this before." A single small lesion persists on the side of the face; otherwise the skin is normal in appearance.

CASE 21.—Dr. J. Frank Frazer, New York, saw a case of lupus erythematosus in which there was an extensive butterfly eruption of the face, with additional lesions on the arms, hands and feet. The duration was two and one-half years on the face and six months on the body. The patient was presented at the January, 1926, meeting of the New York Dermatological Society. He received twenty injections of gold and sodium thiosulphate, beginning with 100 mg. twice a week and the dosage increasing to 150 mg. There was no reaction. At the end of the course, "the eruption on the limbs had disappeared and the facial lesions were very much lighter and free of scales." The patient was again shown

at the April meeting of the New York Dermatological Society. "The members who saw the case at the previous meeting commented on the marked improvement."

CASE 22.—Dr. J. Edgar Fisher, Cleveland, referred one patient for treatment who was cured. Another woman, aged 40, had lupus erythematosus discoides for six years. She received three injections of gold and sodium thiosulphate. After the third injection she developed chills, malaise, nausea, vomiting, elevation of temperature and occipital headaches. "The eruption is now somewhat improved."

CASE 23.—Miss D., aged 35, a patient treated by Dr. W. H. Guy, Pittsburgh, presented an eruption of sixteen years' duration. It began on the nose and

Fig. 7 (case 22).—Lupus erythematosus of the face in one of Dr. Guy's patients; eruption on arms, chest and neck appeared three days after the twentieth injection of gold; the acute eruption resembles a lupus erythematosus and likewise a polymorphic erythema.

spread over the cheeks, involving the entire face. The patient received twenty injections of sodium and gold thiosulphate, 100 mg. twice a week. The condition had improved gradually until only islands of active disease remained. Three days after an injection, on Aug. 28, 1926, the patient developed an eruption over the neck, chest and arms as shown in figure 7.

CASE 24.—Mrs. L. M., aged 50, a patient of Dr. Guy, presented a case of lupus erythematosus affecting the right ear, right side of the scalp and the temple, of twenty-one year's duration. She had been treated with roentgen rays, radium, carbon dioxide and other remedies. There was chronic roentgen-ray dermatitis

on the temple. She has received five injections of gold at three day intervals. "Eruption definitely improved; patient states that she is more comfortable than during the past five years." The treatment is to be continued.

CASE 25.—C. M., aged 22, a patient of Dr. Guy, presented a typical discoid eruption on the chin, nose and cheeks. He has received twelve injections of gold and three local applications. "Patient materially improved but eruption still active."

REACTIONS

Reactive manifestations not infrequently occur after the intravenous use of different gold compounds. They may be, generally speaking, classed under three headings.

1. *Foreign Protein Reaction.*—When colloidal gold is used and a protein is employed to protect the gold, the reaction is commonly a foreign protein reaction, occurring usually after each injection. It frequently begins about an hour after the injection with a dull aching headache, suffusion of the eyes and a chill. The temperature may or may not be elevated. The reaction lasts a half hour or more, and following this the patient feels well.

2. *Toxic Reaction Due to the Gold Compound.*—The symptoms vary in severity according to the compound used and the dose employed. The phenomena appear some hours after the injection and consist of chills, fever, nausea, vomiting, headache and prostration. The fever and malaise may last for two weeks or more. In the cases of patients treated in Germany with rather large doses of gold compounds, diarrhea with bloody stools and severe stomatitis has occurred. A few cases were fatal. (One of my patients had marked abdominal pain and metrorrhagia.) In one case, after a moderate febrile reaction following the second injection, a lupus erythematosus of two years' duration completely disappeared.

Cutaneous reactions: Itching of the skin and in other cases urticaria have at times been observed after gold injections. In some cases after a variable number of injections there is a febrile reaction associated with a "flare up" of the lupus erythematous eruption. All of the clinicians who have observed these reactions express a doubt as to whether one is dealing with a toxic medicamentous eruption, or whether the existing lupus erythematous eruption has been stimulated to extension with the development of new lesions elsewhere. We have seen a few cutaneous reactions and we can appreciate the difficulty of arriving at a definite conclusion on this point. The acute eruption which is induced usually subsides in a few weeks, and is therefore probably not a true lupus erythematosus. In figure 7 from a case observed by Dr. Guy the condition looks like a lupus erythematous extension. In another patient with a lupus erythematosus limited to the face, there was a widespread erythematosquamous dermatitis on the face, neck, arms and legs. This

looked not unlike some cases of arsphenamine dermatitis. It lasted about three or four weeks and then cleared up, leaving the original eruption improved. Some patients develop itching after injections. These cases must be watched closely for fear a dermatitis might develop.

3. *Immediate Reactions.*—These reactions have been described recently after the use of Triphal. Görl and Voight [23] report reactions appearing a few minutes after intravenous injections of this compound. In case 1, a strong girl, aged 20, with lupus erythematosus, received 0.01, 0.025 and 0.025 Gm. of triphal at eight day intervals. Two minutes after the third injection the patient uttered a cry and became unconscious. The pulse and breathing ceased and the patient presented a moribund picture. After artificial respiration, massage of the heart region and stimulants, the pulse gradually became palpable after one half to three quarters of an hour. The patient could not see and she had a severe pain in the leg. Three hours later, there were vomiting and diarrhea. Nine hours after the injection a right-sided hemiplegia set in (perhaps because of the circulatory disturbance following the cardiac weakness). The paralysis slowly regressed in the course of a few weeks.

In case 2, a strong woman, aged 50, with psoriasis, had received 0.001, 0.005 and 0.01 Gm. of this drug at eight day intervals. One-half minute after third injection, the patient complained of a thick feeling in the head and severe pains in the hands, and then in the lower part of the abdomen and the feet. The patient was given two injections of camphor. A short time later, amnesia developed. In the afternoon, vomiting occurred. There was no influence on the psoriasis. Three other patients developed somewhat similar symptoms. The product was apparently dispensed in solution.

It is obvious that these reactions are not due to the gold in the compound, but either to some impurity or to some dissociation of the compound which produces a physical change in the blood or the blood vessels. We have never observed reactions of this type after the use of gold and sodium thiosulphate.

VARIATION IN SUSCEPTIBILITY TO REACTIONS

As is the case with various other metallic compounds, notably the arsphenamines, a great variation in susceptibility exists on the part of different patients as to their tolerance to gold. Some patients will develop a febrile reaction after the first or second injection, whereas others will tolerate apparently an unlimited number of injections. One of our patients (in case 6) has received more than 100 gold injections given twice a week during the period of a year. She has never had a reaction.

23. Görl and Voigt: München. med. Wchnschr. **33**:1360, 1926.

This difference in tolerance suggests the caution that the first injection of gold and sodium thiosulphate should not exceed 50 mg. After this the dose can be increased to 100 mg.

TOXICITY

The toxicity of different gold compounds varies not only according to the percentage of contained gold but also according to the chemical constitution of the molecules. We have on several occasions tested out the toxicity of sodium and gold thiosulphate and have compared the same with Krysolgan. The figures are as follows: Sodium and gold thiosulphate is tolerated intravenously in rats in doses of 35 mg. per kilogram. Krysolgan is tolerated in doses of 20 mg. per kilogram. The former, therefore, is distinctly less toxic even when the difference in gold content is considered. The latter contains, according to our analysis, about 55 per cent of gold, and gold and sodium thiosulphate about 38 per cent.

Møllgard [24] gives the toxicity of sodium and gold thiosulphate in various mammals as follows: mice (subcutaneous), 12 cg.; guinea-pigs (intraperitoneal) from 2 to 4 cg.; rabbits (intravenous), 4 cg.; rabbits (subcutaneous), 8 cg.; goats (intravenous), 3 cg.; calves (intravenous), 6 cg.; macacus sinicus (intraperitoneal), 6 cg. per kilogram of weight. It is rather remarkable that the higher mammals of larger size should tolerate proportionately larger doses than the smaller animals. This is the reverse of what takes place with mercury and arsenic.

Gold is largely eliminated through the kidneys and only a relatively small percentage is excreted through the intestines, according to Møllgard. Gold is found in the urine for from four to six days after the administration of a 1 Gm. dose to a calf, whereas in the intestinal contents only traces are found twenty-four hours after the administration. The renal elimination of gold is seen to be relatively slow.

Dewitt, Caldwell and Leavell [25] determined the distribution of gold in the organs of guinea-pigs after administration by mouth and after subcutaneous and intracardiac injections. The largest amounts were found in the liver, intestines and skin. Møllgard, on the other hand, found infinitely more in the kidneys of calves than in the intestines after intravenous injections.

Brown, Saleeby and Schamberg [26] studied the toxic effects of certain gold compounds as indicated by the blood chemistry and pathologic changes in the organs. It was found that histologic changes of a pronounced type may take place in the kidneys before the blood picture

24. Møllgard (footnote 20, p. 45).

25. DeWitt, Caldwell and Leavell: J. Infect. Dis. **23**:425, 1918.

26. Brown, Saleeby and Schamberg: J. Pharmacol. & Exper. Therapy. **11**:357, 1918.

shows definite changes. Møllgard states that "Sanocrysin has never been found to have any injurious effect on the liver," and that "microscopic examinations of the livers of animals treated with high doses never show any degeneration or destruction of liver cells." The foregoing investigators found extensive liver changes after five doses of 30 mg., six doses of 50 mg. and one of 70 mg. per kilogram in rabbits. It is true that these are high doses, far above the therapeutic limit.

Heubner believes that gold has a toxic effect on the capillary endothelium. Stuhl supports this view and states that even after small doses of Krysolgan he has seen menorrhagia, and abortive and climacteric bleeding. He attributes these results to the injury of small capillaries in the uterus.

Feldt does not accept Heubner's theory. He believes that gold acts in the patient as a catalyst. The specific and nonspecific protective bodies in the diseased areas are set free and exert a damaging effect on the tubercle bacillus.

Rickmann [17] from observation of the effects of gold in tuberculous laryngitis is of the opinion that, no matter which theory is correct, the connective tissue development in tuberculous granulation tissue is stimulated and that nature's healing method is hastened.

In this connection it is interesting to quote the statement of Wells, DeWitt and Long [27] that "other drugs, notably certain gold compounds, excite a hyperemia of the tissue surrounding the tubercles and cause a reaction resembling that of tuberculin, the results being beneficial or otherwise, depending upon the degree of the reaction."

COMMENT

From the foregoing it will be seen that in the gold treatment of lupus erythematosus we possess a systemic remedy of real efficacy. When one considers how refractory and unresponsive to therapeutic endeavor lupus erythematosus has been in the past, the results now achieved are all the more gratifying. A number of patients here reported on were subjected during years of futile effort to roentgen-ray and radium treatment not only with no curative effect, but with a certain amount of injury to the tissues, rendering the condition less amenable to subsequent therapeutic methods.

In nearly one half of the patients treated the eruption has disappeared or has virtually cleared up. The great majority of the remaining patients are improved and are still under treatment. Some of the timid and less cooperative patients have discontinued treatment because of unpleasant reactions.

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27. Wells, DeWitt and Long: The Chemistry of Tuberculosis, Baltimore, Williams & Wilkins Co., 1923.

We are still in doubt as to some technical features of the treatment; i. e., concerning dosage, frequency of administration, duration of treatment, etc. We believe that sodium and gold thiosulphate, the compound so thoroughly studied by Møllgard and his associates for use in systemic tuberculosis, is the most eligible preparation of gold known at present for intravenous use. We give, however, much smaller doses than are advocated by Møllgard. Our experience thus far leads us to believe that it is wise to begin with conservative dosage and, after testing the patient's tolerance, to increase cautiously the amount of the drug administered. How high the individual dose can be increased in cases that are not responding well we do not yet know. We begin with an initial dose of 50 mg. dissolved in 2 cc. of sterile distilled water. If well tolerated, we then give a second injection from five to seven days later of 100 mg. These are continued at weekly intervals. In some cases we have given 100 mg. twice a week, but in view of the greater liability to severe reactions with perhaps the stimulation of a lupus erythematous outbreak, we have resorted to this only after mature deliberation and study. As has been stated, patients vary enormously in their susceptibility to gold. One patient may develop a febrile reaction after a few weekly doses of the drug, whereas others may take the drug once or twice a week over many months. We have furnished some of our compound to a colleague for trial in pulmonary tuberculosis. In several cases doses of 200 mg. were given twice a week. Doses of 300 mg. were likewise given once a week, and through an inadvertence 600 mg. once a week for four weeks. Malaise and general depression resulted. Albuminuria was observed in some of these cases, and likewise itching and urticaria.

In Copenhagen it is not uncommon to reach a dose of 1.0 Gm., or in exceptional cases 1.5 Gm. in the treatment of tuberculosis. Severe reactions are induced with albuminuria and, at times, the presence of granular and blood casts in the urine. Not infrequently a moribilliform, scarlatiniform or polymorphous erythematous eruption, or a generalized dermatitis develops. As the largest dose that can be given with safety in rats is 35 mg. per kilogram, or the equivalent of 2,100 mg. for a man weighing 60 Kg., it would appear to us hazardous in inject 1,000 or 1,500 mg. into a human being, particularly when the injection is repeated. While some patients exhibit marked improvement after a febrile reaction, such a constitutional disturbance is not essential to improvement or cure.

Great care is necessary in treatment in cases of the disseminate type, and in these cases the initial dose should not be over 25 mg., gradually increasing to 50 mg., and perhaps to 100 mg. We believe that in one patient a fatal acute outbreak was stimulated, although a year or two before the patient had had a rather severe attack of a similar though

less extensive character. Gold acts in these cases as tuberculin does in certain frankly tuberculous conditions.

After the disappearance of a lupus eruption it is well to give the patient a month's rest, and then to give some additional injections as security treatment to prevent a relapse. We have known such relapses to take place when the supplementary treatment was not given.

We have observed in a number of cases a focal reaction in the affected areas, with the production of increased reddening, stinging and burning. We believe that it is unwise to use gold in pregnant women as we observed metrorrhagia and "labor-like" pains after a few injections in a young married woman; Stuhl has likewise reported uterine bleeding. As to the mode of action of gold in lupus erythematosus nothing of a positive character can be stated. The interesting query arises, "Does the almost specific effect of gold treatment in lupus erythematosus forge another link in the imperfect chain of evidence pointing toward the tuberculous origin of the disease?" Perhaps. We are content in this communication to present the factual observations and to leave speculation to future developments.

It is interesting in this connection to note that we have secured a prompt healing of a refractory and rather extensive tuberculous ulceration of the foot with gold treatment. The condition later relapsed but again yielded promptly on the resumption of treatment. Generally speaking, lupus vulgaris is not as amenable to treatment with gold as lupus erythematosus, although cases reported in the literature have improved after treatment with some of the older gold compounds.

MICROSCOPIC CHANGES IN VARIOLA*

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AND

KANO IKEDA, M.D.

MINNEAPOLIS

The causative agent of smallpox is not positively known, but many facts about its nature have been learned, and the effect of its action on the epidermis has been carefully observed.

In former years, many bacteria isolated in smallpox cases were described as the cause of this disease. Today, however, the presence of these bacteria is looked on as accidental, while the contents of variola vesicles are usually free from bacteria. The disease can be transmitted with inoculations of this clear, bacteria-free fluid, and passage through a Berkefeld filter does not destroy the potency. In the severe forms of smallpox, streptococci have been found frequently in lesions and in the blood stream. The investigations of Hines [1] in the Chicago epidemic of 1922, using the modern grouping, showed the presence of both hemolytic and nonhemolytic streptococci. Arndt [2] in a careful study of the Dresden epidemic of 1918-1919 found streptococci and pneumococci in blood cultures. Despite this and a great many citations from the literature, the majority of investigators look on bacteria as secondary invaders and do not take them into consideration as factors in producing variola, but they do concede a symbiosis of the variola virus with streptococci in the severe, often fatal, cases.

Paschen [3] describes and gives many interesting facts concerning the causative agent of smallpox in his monograph on variola. He states that the cause of smallpox must be a living organism because the smallest amount of content from a smallpox pustule when implanted on another person can produce the disease. He defines the causative agent as a minute, round, coccus-like body which divides amitotically and does not stain with ordinary dyes, but is present in large quantities in small-

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* From the Division of Dermatology, University of Minnesota, and the Minneapolis General Hospital.

* Read at the Golden Anniversary Meeting of the American Dermatological Association, Philadelphia, May, 1926.

1. Hines, L. E.: The Bacteriology of the Skin Lesions in Small-Pox, J. Infect. Dis. **31**:89, 1922.

2. Arndt, T.: Die Pockenepidemic 1918-19 in Dresden, Ergebn. d. inn. Med. u. Kinderh. **20**:524, 1921.

3. Paschen, E.: Die Pocken, in Jochmann-Hegler: Lehrbuch der Infektionskrankheiten, Berlin, 1924, p. 843.

pox lesions and readily passes through a Berkefeld filter. Cultures have not yet been made, but apparently it is an obligate cell parasite which requires the living epithelial cell for its development and multiplication. The so-called inclusion bodies have been variously described as the chlamydozoan variolae vaccinae of Prowajek, or the elementary corpuscles of Paschen, and probably are related closely to the Guarnieri bodies which have been the subject of a vast amount of investigation and literature.

Pfeiffer was the first to describe exactly the peculiar bodies found in the epithelial cells in smallpox lesions. He also attributed a protozoan character to these bodies, which were later called vaccine corpuscles. Guarnieri [4] showed that if the cornea of a rabbit were scarified and inoculated with variola or vaccine lymph, in about thirty hours epithelial thickening occurred, which in three days ulcerated; and if this ulcer were studied microscopically, small, variously shaped, deeply staining nuclear bodies were found lying in the epithelial cells. From his work the bodies are now generally known as Guarnieri bodies.

Councilman [5] and his co-workers, in an elaborate research during the Boston epidemic of 1901-1903, fully described these bodies and looked on them as parasites which were the cause of smallpox and vaccinia. Paschen opposed the supposition of Guarnieri that this so-called parasite body penetrated the epithelial cell and rested in the vicinity of the nucleus, finally destroying it. He also opposed Gins who viewed the Guarnieri body as an independent foreign invader which might also be found between the epithelial cells. Paschen looked on these bodies as a product of cell reaction to the causative agent rather than a parasite which could produce smallpox. He has demonstrated that the virus of variola will pass through the Berkefeld filter, while the Guarnieri body will not, and he cited the conclusive experiments of Foa who showed that the Guarnieri body could be damaged by treating the lymph with certain chemicals without, however, destroying its potency.

In almost all of our preparations we were able to find areas that showed many inclusion bodies. They varied decidedly in number but were of uniform size. They were perfectly round, colored deep blue with hematoxylin and were found most often in the middle epithelial layers within the cells in the vicinity of the nucleus. The cells in which

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4. Guarnieri, G.: Recerche sulla Patogenesi ed Etiologia delli'infezione vaccinica e variolosa, Arch. per le sc. med. **26**:403, 1892, quoted by Councilman; Ueber die Parasiten der Variola und der Vakine, Centralbl. f. Bakteriol. **16**:894, 1891.

5. Councilman, W. T., et al.: Small-Pox Studies, J. M. Research, **11**:12, 1904.

the bodies were found often showed a clear cytoplasm, and the nucleus in some preparations appeared unaltered, while in others it stained poorly, appeared granular and in certain sections was decidedly condensed or even apparently in fragments. Inclusion bodies were found frequently in cells that were undergoing ballooning degeneration.

THE PAUL TEST

Whether or not the Guarnieri body is the causative agent or the evidence of a cell reaction to this agent, its presence lead Paul [6] to devise a valuable diagnostic test for the differentiation of variola from varicella. The test is particularly valuable in diagnosing cases which cannot be differentiated on purely clinical grounds, especially in sporadic cases, in which an early diagnosis may avert an epidemic by the prompt employment of isolation and general vaccination. In brief the test is performed as follows: The lesion is cleansed with alcohol and opened with a sterile needle; the fluid content is mounted on a cover slip which may be sent to the diagnostic laboratory (drying does not destroy the potency of smallpox lymph). If the pustular stage is past, crusts or scabs may be removed and used. At the laboratory the secretion is emulsified in physiologic sodium chloride solution. Both eyes of a rabbit are cocainized and delicately scarified with a fine needle in both vertical and horizontal directions, in the form of a small gridiron. A drop of the emulsion is rubbed gently over the scarified cornea of one eye, the other serving as a control. After thirty-six hours, a variolated cornea shows definite changes macroscopically. Minute elevations can be noted which with a lens may show central depression. These little elevations cannot be wiped off. The observation is not complete, however, with the discovery of these specks. In forty-eight hours the rabbit is chloroformed, and the eyes enucleated and placed in sublimate alcohol. In a few minutes a variola infected cornea will show isolated or confluent intensely white opaque elevations. The uninoculated eye may show a few faint lines but no protuberances. This phenomenon, according to Paul, is pathognomonic for variola. He has used the contents of varicella and impetigo contagiosa blebs which always gave negative results. Tanda [7] confirmed the test and obtained negative results in varicella and erythema multiforme. Scott and Simon [8] used the test in

6. Paul, Gustav: Objektive Sicherung der Varioladiagnose durch den Tierversuch, Wien. med. Wchnschr. **29**:862, 1916.

7. Tanda, G.: Corneal Inoculation by Paul's Method for the Differential Diagnosis Between Small-Pox and Chicken-Pox; abstr., Igiene mod. **15**:172 (June) 1922.

8. Scott, J. M., and Simon, C. E.: The Diagnosis of Small-Pox by the Paul Method, Am. J. Hyg. **3**:401 (July) 1923.

America and regarded it as a valuable diagnostic aid, especially when controlled by examinations of the microscopic changes, which in positive cases on sagittal section show epithelial thickenings. In these areas Paul [9] has demonstrated Guarnieri bodies. Gins,[10] in the Robert Koch Institute, has carried out the test many times and has emphasized the fact that the dry secretion is potent even when preserved for more than a week. The Prussian government in 1916 made the Paul test obligatory in suspected cases.

Kyrle [11] has described inclusion bodies in psoriasis vulgaris, which he calls Guarnieri-Psoriasis bodies. We hope to apply the Paul test using psoriasis material in the near future.

Fig. 1.—Positive inoculation of rabbit's cornea (after Paul).

THE PASCHEN TEST

Paschen developed a method whereby his so-called elementary corpuscles could be stained and identified. He believed his method was quicker and just as certain as the Paul test in diagnosing suspected cases of smallpox. His method is as follows: A lesion is opened with the edge of a cover slip, and the contents, down through the basal cells, are spread on the slide just as in making a blood smear. The preparation is dried and fixed in alcohol, stained with hot Loeffler's solution, washed and counterstained with Ziehl's carbol-fuchsin solution. By this

9. Paul, G.: Zur histologische Technik des Kornealversuch bei Pockendiagnose, Deutsche med. Wchnschr. **43**:900, 1917.

10. Gins, H. A.: Erfahrungen mit der experimentallen Pockendiagnose nach Paul, Deutsche med. Wchnschr. **42**:1118, 1916.

11. Kyrle, J.: Histo-Biologie der Mensch, Haut und Ihrer Erkrankheiten **1**:171, 1925.

method the elementary bodies, Paschen says, are found in almost pure culture, and their presence is diagnostic of smallpox.

Many observers have verified the work of Prowajek and Paschen concerning these bodies, and most of them agree that they are intimately connected with, or actually are, the causative agent of smallpox. The final proof of cultivation has not yet been accomplished.

THE HISTOLOGY OF VARIOLA

That the virus of smallpox is carried by the blood has been proved definitely by Kyrle and Morawetz [12] who inoculated the blood of variola patients directly into the veins of monkeys and could produce typical exanthems which ran a characteristic clinical course. The virus is

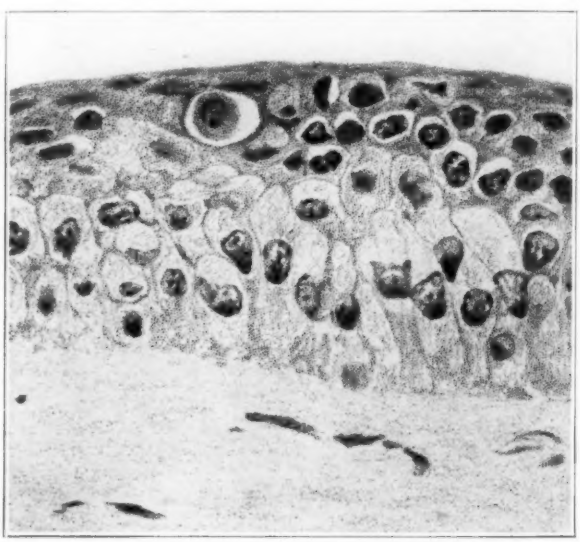

Fig. 2.—Microscopic section of figure 1 (after Paul).

undoubtedly carried into the papillary body and thence into the epidermis where it develops rapidly and brings about a chronologic series of typical changes in the epithelium. Secondary invasion takes place early, and the histologic picture is further changed because of this.

MATERIAL

It is obviously difficult to obtain tissue in the prodromal and early periods of the eruption. The following histologic description is from a study of skin specimens obtained from forty-seven cases of smallpox

12. Morawetz, G., and Kyrle, J.: Variola-Vaccina Immunity, Wien. klin. Wchnschr. **35**:580 (June 24) 1922.

at necropsy. The specimens were excised post mortem from the lateral chest wall and fixed in 10 per cent formaldehyde solution. One specimen of a pharyngeal lesion was secured also. Tissue was obtained from patients who died as early as the third day of the disease and as late as the twenty-third day. In addition to the postmortem specimens procured during the epidemic of 1925, we were fortunate in obtaining biopsy specimens from a sporadic discrete case (April, 1926). Two vesicles on the third day and an umbilicated pustule on the fifth day of the eruption were excised, fixed in a 10 per cent solution of formaldehyde and serially sectioned. In all cases in which we thought it advisable the sections were stained with hematoxylin-eosin, van Gieson, Weigert, Mallory and Verhoeff elastic tissue stains, Dominici and Pappenheim's stains and Gram-Weigert's fibrin stain.

We also obtained biopsy specimens from scars occurring on the face of two patients who had recovered from severe confluent smallpox in 1925.

In studying a vast number of sections from a comprehensive number of cases, one is struck immediately with the extreme variation in the histologic picture; although the fundamental changes are undoubtedly the same, individual variation is great, and the histologic change apparently is not dependent on the severity of the clinical symptoms. Furthermore, macroscopic classification and microscopic observation do not agree. What appeared to be a clinical vesicle, would prove on section to be a distinct pustule, and what was clinically a typical hemorrhagic pustule, microscopically was a vesicle with subcutaneous hemorrhage immediately beneath it. Therefore, we believe that although for practical purposes the clinician may divide the eruption into its various phases microscopically, the process is not so exact.

In the histology of variola it is important to differentiate those earlier changes which are truly specific and are brought about by the action of the virus and those later changes which are caused by secondary invasion.

THE VESICLE

Kyrle [11] stated that the first changes noted in variola were a rete hypertrophy and the formation of inclusion bodies. These changes, he stated, preceded degenerative changes or inflammation of the corium. He believed that variola and psoriasis vulgaris began in a like manner and had in common a number of early pathologic changes.

The earliest change noted in our serial sections was a slight edema of the papillary body. This was sufficient to alter its shape, the tip being disrupted and distorted. Clumps of cells rich in protoplasm, with deeply staining round nuclei, were found in and around the nearby

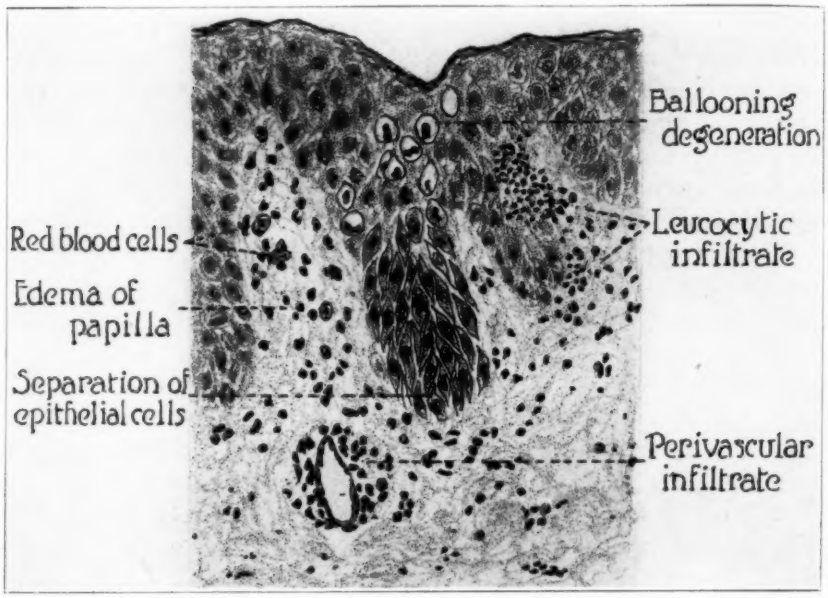

Fig. 3.—Stage 1; vesicle.

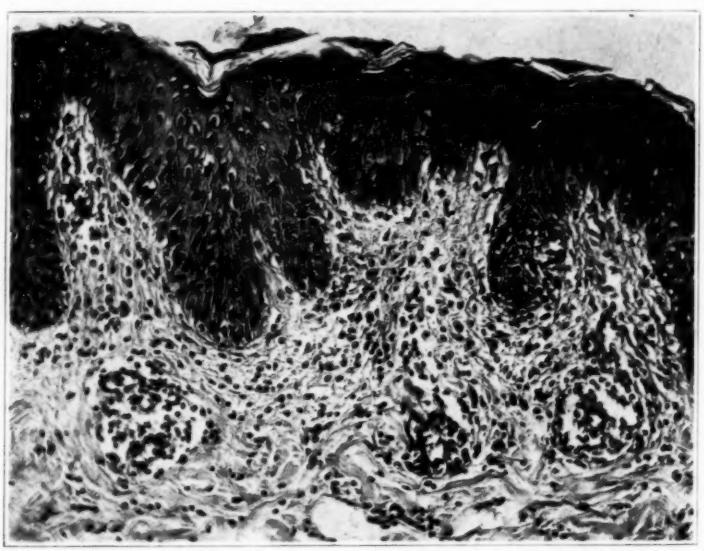

Fig. 4.—Low power magnification of an early vesicle showing perivascular infiltrate, edema and slight vacuolization of the epithelium.

capillaries and in the lymph spaces. The cytoplasm in many of these cells remained blue with the Pappenheim stain; nevertheless, a large number of them were plasma cells with typical nuclei and cytoplasm. Practically no polymorphonuclear leukocytes were found in the infiltrate of the earliest lesions. A curious fact noted was that in the biopsy specimens from the mild discrete case the corium was much more infiltrated with leukocytes than in most of the postmortem specimens. In certain areas these cells penetrated between the basal cells making dense cellular projections. Free red blood corpuscles were present at the very tip of some of the edematous papillae, and in these particular sections many corpuscles were found also in and around the adjacent

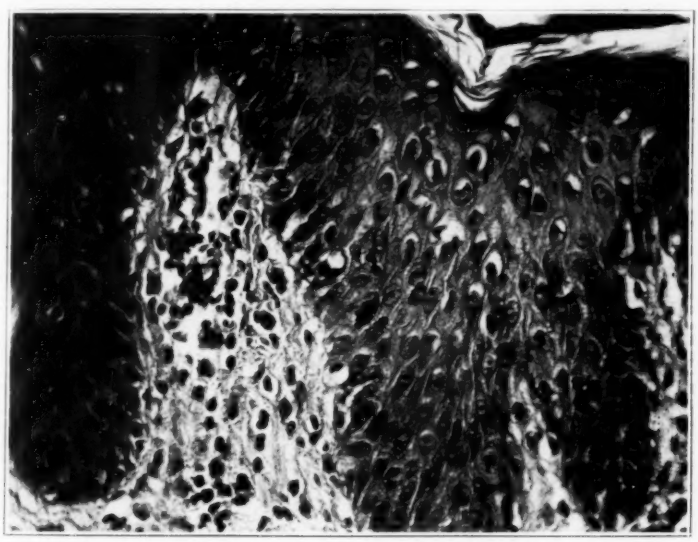

Fig. 5.—High power magnification of an early vesicle showing edema of papilla with extravasation of red blood cells, a few leukocytes and ballooning of the epithelium cells.

capillaries. When the edema was marked the lymph passed up between the basal cells, tearing the cells apart, the rift going upward so that little perpendicular canals were formed between the tiers of cells. The cohesion between individual cells was lost. This was particularly noted at the center of the pocks. At the periphery the cells seemed to remain firmly cemented, but there was a decided change in the cytoplasm and nuclei, which was not uniform. An area of cell degeneration alternated with an area in which there was only slight cell change. In some sections these areas were separated by a cone of leukocytes which were an upright projection from a dense infiltrate in the under-

lying lymph space. The entire epithelium except the corneal layer overlying the involved basal area seemed to participate in the early changes.

The basal cells in the biopsy specimens from the benign case were more severely attacked by the virus than those in any of the postmortem specimens. Here in some areas the cells showed a peculiar lengthening of their nuclei, which stained more faintly and showed many granules. In other areas the basal cells became round and swollen, looking like little balls, or showed a clear zone immediately surrounding the nucleus.

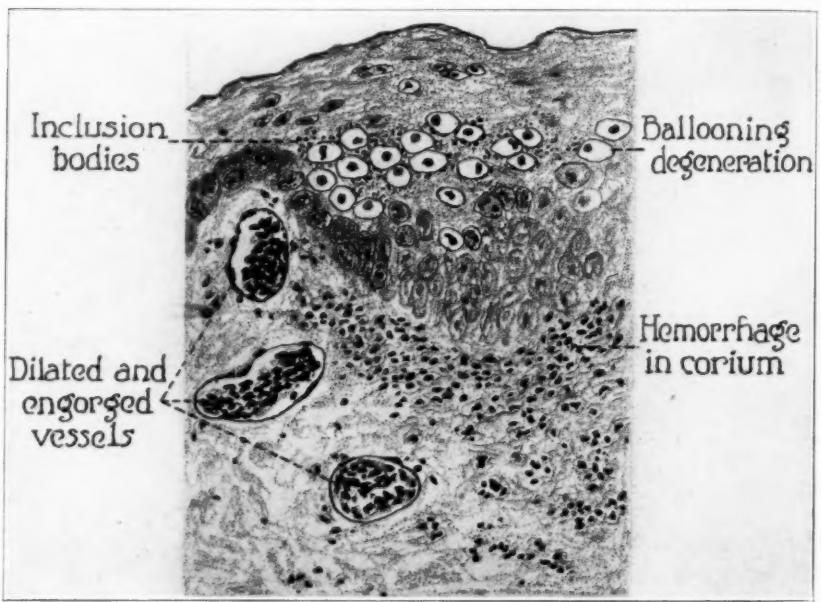

Fig. 6.—Stage 2; purpuric vesicle.

On the other hand, in the severe, early fatal purpuric cases we usually found an entirely intact basal layer, with the layers immediately above showing typical ballooning changes. In fact, this was so striking that until we examined the biopsy specimens we had decided that the basal cells were resistant to the action of the virus and concluded that the cells of the malpighian layers were the earliest ones affected. This we can now state is not constant. We believe that no particular layer of the epithelium has a predilection, but that the virus may affect only certain layers or all of the layers at the same time, there being a decided individual variation.

Ballooning degeneration as described by Unna, however, is found more constantly in the lower malpighian layers. This type of change,

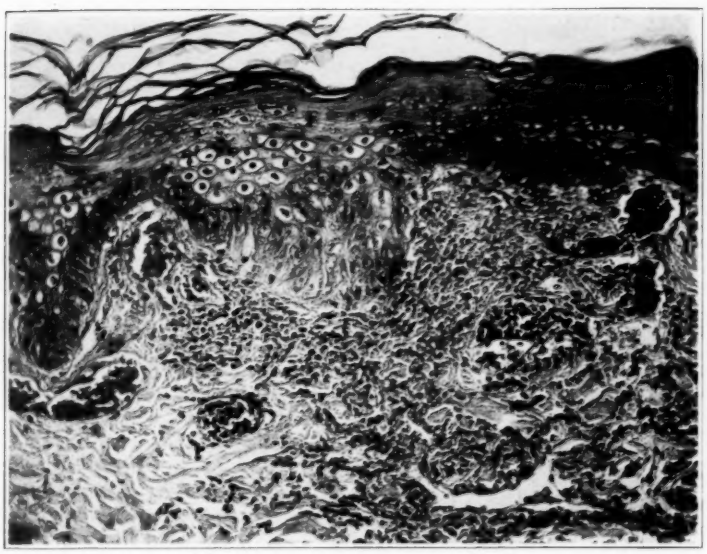

Fig. 7.—Early vesicle showing marked ballooning of epithelial cells, perivascular infiltrate and hemorrhage into the corium.

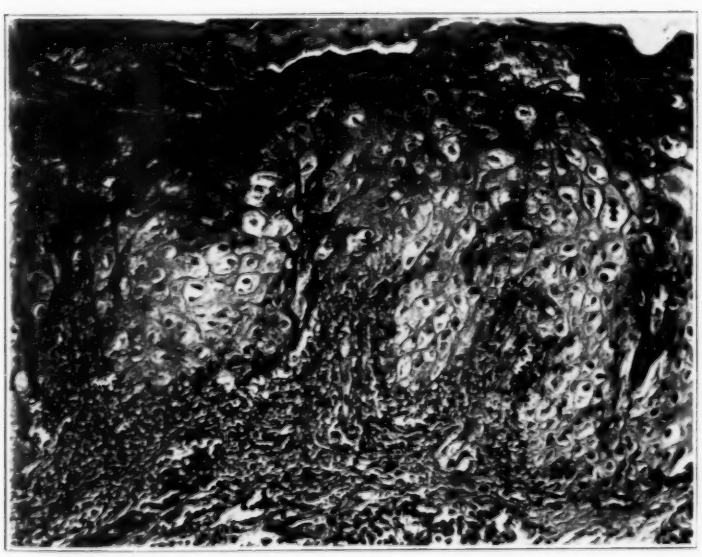

Fig. 8.—High power reproduction of figure 7.

although ever present to some degree in our sections, is by no means distinctive of the variola process, but is found in many other cutaneous conditions which are characterized by vesicle formation. Councilman looked on this as a form of hyaline fibrinoid degeneration, which is identified by a clear space forming around the nucleus, which extends peripherally, reducing the cytoplasm to a mere thin network. The cells become almost perfectly round in outline, apparently lose their prickles and lie like balloons in the spaces that are formed. The nuclei become smaller—some become round and take a deep stain, while others become shrunken, assume odd nondescript shapes and stain poorly. Sometimes

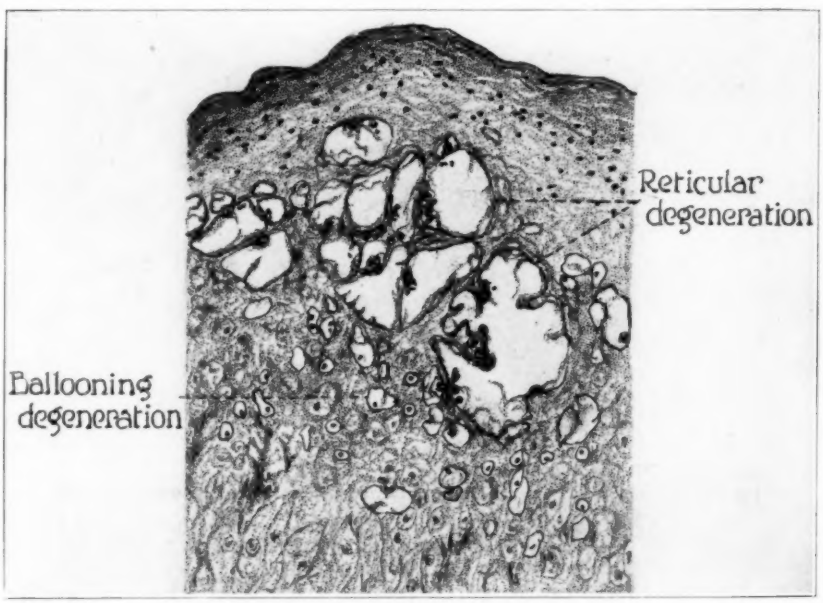

Fig. 9.—Stage 3.

several nuclei were seen within a clear circumnuclear space. Many inclusion bodies were seen in these spaces as well as in the periphery of the ballooning cells.

Typical reticular degeneration or colliquative vesiculation was found in the middle of the epithelium. In early lesions isolated vacuoles were noted, sometimes only a few, and in other areas many. The vacuoles were of various sizes but always oval or round in outline, or from their shape it was evident that several smaller vacuoles had coalesced into an irregular space. A network remained making a meshwork between the vacuoles. Many of the individual cells had lost their prickles or apparently had undergone liquefaction, or the tension of the accumulated exudate had torn them asunder making spaces. Various types of cells,

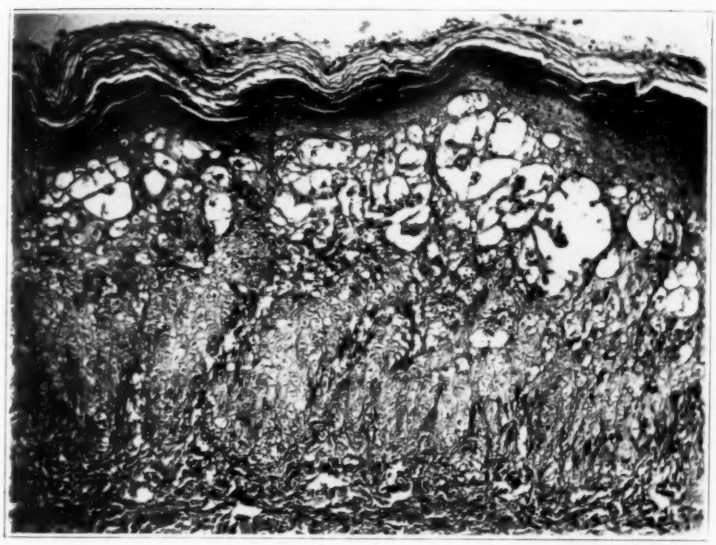

Fig. 10.—Low power magnification of a late vesicle, showing reticular degeneration.

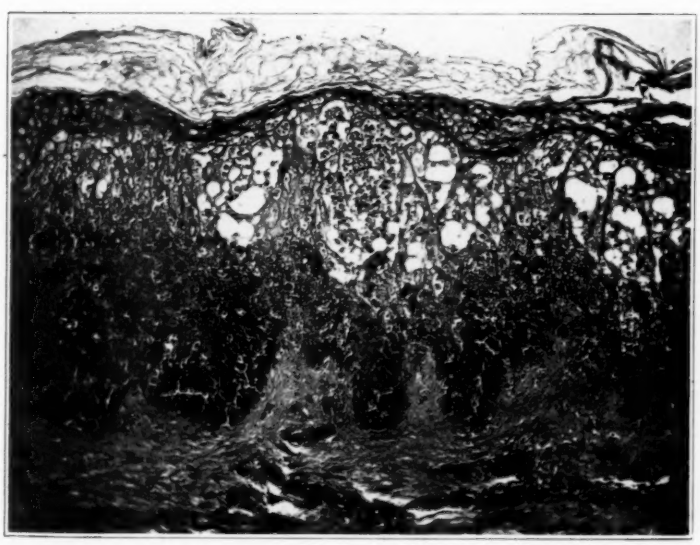

Fig. 11.—Low power magnification of an early pustule showing invasion of polymorphonuclear cells into reticular spaces.

cell remnants and a coagulable homogenous material, as well as inclusion bodies, were found in the spaces or enmeshed in the septums of this chamber work.

In certain sections this reticulation involved the corneal layers. There were superficial chambers with septums made up of corneal cells which were overlying similar chambers in the malpighian layer. Here and there communication had been established between the superficial and the deeper chambers, but there was always a fairly strong corneal roof over all.

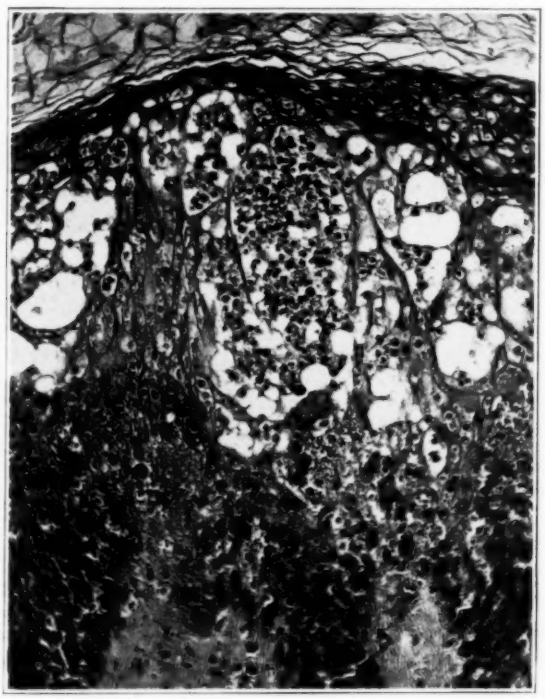

Fig. 12.—High power reproduction of figure 11.

From our serial sections we were able to ascertain that the pock cavity had the form of a mushroom whose upper projecting portion came to a sharp margin.

The overhanging portion of the cavity rested on a cushion of hyperplastic epithelial cells. The peripheral proliferation took place simultaneously with the central degeneration. The cells of the prickle layer were enlarged, edematous and swollen in appearance. The cords of cells inclined toward the cavity, making a rounded, edematous but solid surrounding wall or body. The peripheral portion of the cavity

rested on this while the base of the central portion of the cavity depended on the depth of the degenerative process. In some pocks the entire basal layer was destroyed, and the center of the pock had the bare inflamed corium for its base. In this type umbilication or central dell formation could be explained easily. The periphery was buoyed up by the edematous lateral pock body while the central portion sunk because of the liquefied and degenerated epithelium. We do not think that a central sebaceous or sweat duct caused umbilication. We followed one lesion serially that had a sebaceous duct in its center, but there did not seem to be any sinking because of it although the epithelium of the sebaceous apparatus took part in the typical variolous change. In other pocks

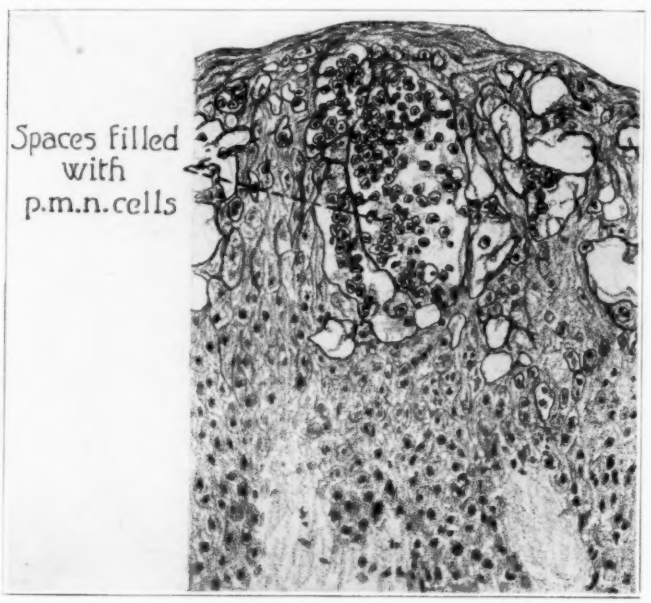

Fig. 13.—Stage 4; early pustule.

the basal layer remained intact. Here umbilication may have been produced by the extreme hyperplasia and edema of the peripheral portion, or by condensation of the contents.

No epithelial giant cells as were described by Hammerschmidt [13] in varicella were found.

THE PUSTULE

The change of the smallpox vesicle into a postule takes place early in the course of the disease, earlier microscopically than macroscopically. It is brought about by an influx of polymorphonuclear leukocytes

13. Hammerschmidt, Johann: Histologische Befunde bei Varicellen, Beitr. z. path. Anat. u. z. allg. Pathol. **65**:346, 1918.

probably attracted by the degenerated tissue. The clear homogenous substance that fills the earliest lesions soon becomes very cellular. The spaces contain tissue débris and dense collections of leukocytes. The pustule is often multilocular. In some sections we found one chamber of a lesion packed full of polymorphonuclear cells while an adjacent cavity contained only a little serum and ballooned cells. The older pustules tend to become unilocular or the exudate apparently solidifies, compressing the cells, detritus and remaining tissue into one solid mass.

We also found another form of pustule which occurred in the benign discrete case of smallpox. This particular lesion was excised on the third day of the disease; a similar but somewhat more advanced lesion was excised on the fifth day. An acute destructive type of diffuse infiltrate was found in the papillary and subpapillary portion of the corium in this type of pustule. The epithelium from the basal layer

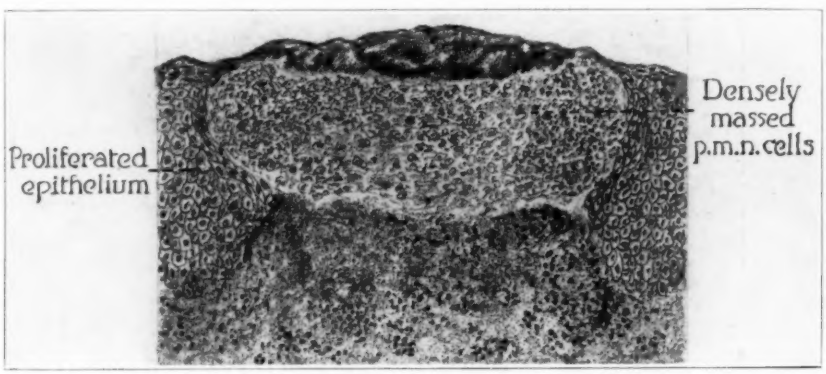

Fig. 14.—Stage 5; advanced pustule.

through to the corneal cells was completely destroyed and replaced by an hour glass shaped cone of purulent exudate. There apparently was little roof over the lesion and the bottom was confluent with the subepithelial infiltrate. At the periphery there was a slight hyperplasia of the prickle cells. Many of the cells showed a clear zone about the nucleus, but degeneration had not gone further. The lesions microscopically had the appearance of certain pustular syphilids which we have examined; and we have seen sections of acute papulonecrotic tuberculids which also resembled them. In the cells of the periphery, inclusion bodies were noted frequently.

LESIONS OF THE MUCOUS MEMBRANE

Councilman, Poleff and others have described the pathologic condition of lesions occurring in the mucous membranes. Diffuse diphtheritic lesions, as well as typical variola lesions, were observed frequently early

in the course of the disease. Prowajek described a type of lesion which he called the protopustule. He believed that this lesion occurred before the general exanthem and that this protopustule played an important rôle in the dissemination of the disease.

In general, mucous membrane lesions resemble those of the skin in the ordinary case. They probably develop more rapidly than skin lesions for they are observed only in the early days of the disease. The loose character of the tissues, the greater vascularity and the lack of

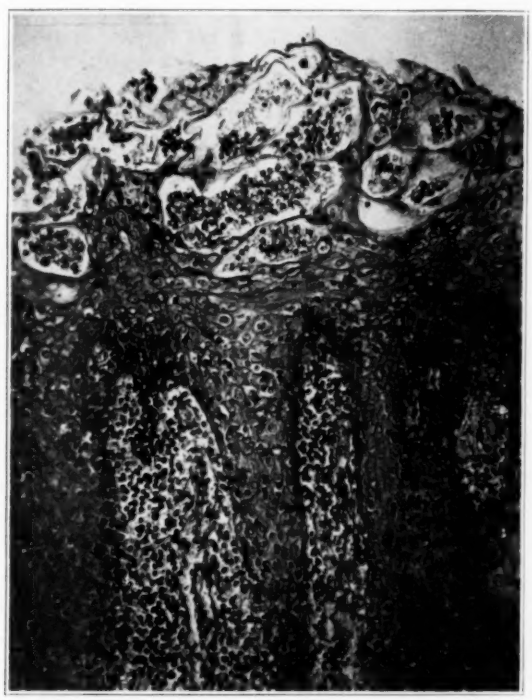

Fig. 15.—Details of mucous membrane pustule.

an impervious corneal layer are the factors that facilitate their rapid course.

The single pharyngeal lesion that we examined was clinically and microscopically a pustule. It showed superficial multilocular chambers. The surface was frayed out, some of the chambers having practically no roof, or only a thin membrane, which evidently was composed of the remnants of cells or reticulum. Many superficial cells apparently were exfoliating. The chambers of the pustule were filled with polymorphonuclear leukocytes. The lower layers of the epithelium showed ballooning degeneration while the subepithelial infiltrate was extensive and of

the purulent type. In the main, the lesion greatly resembled the same stage of pustule in the skin and had specific characters enough present to identify it. Inclusion bodies were found there also.

HISTOLOGY OF THE HEMORRHAGIC FORMS

One of us [14] (Ikeda) has proposed dividing the hemorrhagic forms of variola into three types. The classification is based on the histologic observations and the blood picture.

1. *Hemorrhagic Pustular Form.*—Clinically this form was recognized by hemorrhages apparently in or under fully developed typical pustules. Microscopically, pustules of variola were found in various stages of

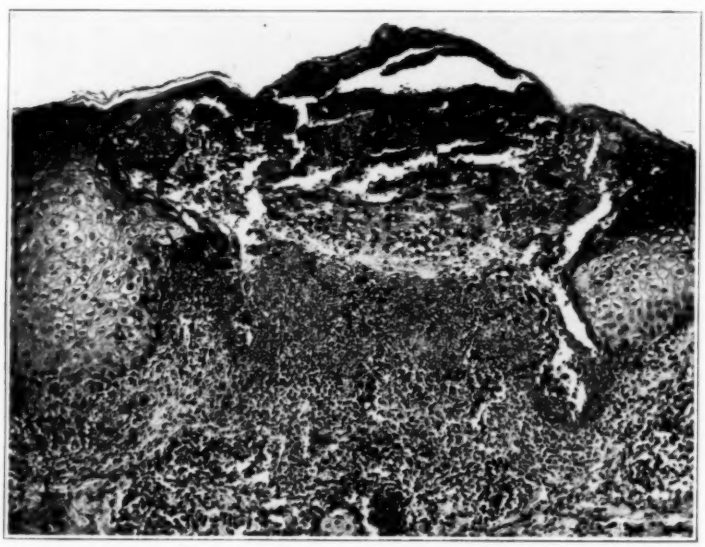

Fig. 16.—Low power magnification of a late pustule showing pock body and dense pustular infiltrate.

development, most often fully grown, with evidences of beginning epithelial repair. There was superimposed an active exudative inflammation of the subpustular tissues with intense edema, hyperemia and some extravasation of blood, especially at the base of the pustule, rarely directly into the pock cavity. In this type no diffuse hemorrhages in the adjacent unaltered corium or subcutaneous areas were found.

The blood observations were those of severe pustular smallpox.

2. *Primary Purpuric.*—Clinically this type is characterized by a diffuse purpura which begins as an intense cherry colored erysipeloid

14. Ikeda, Kano: The Blood in Purpuric Smallpox (Clinical Review of Forty-Eight Cases), J. A. M. A. **84**:1807-1813 (June 13) 1925.

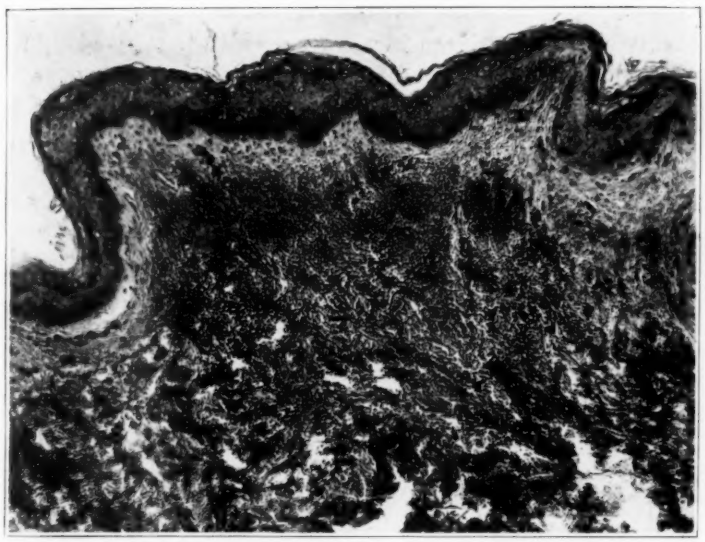

Fig. 17.—Primary purpuric type of smallpox showing slight change in the epithelium and dense diffuse hemorrhage in the corium.

Fig. 18.—Secondary purpuric type, showing early vacuolization in the epithelium, dilated blood vessels and extravasation of red blood cells.

erythema, which early shows marked extensive subcuticular and submucous extravasations of the blood and severe constitutional disturbance terminating lethally after a short stormy course. Microscopically, the epithelium overlying hemorrhagic areas may or may not show early variola changes. If present, only slight ballooning of the cells of the middle epithelial layers or early vesicle formation, but no advanced changes, are encountered. In many areas the epithelium was apparently entirely normal over the purpuric spaces. The entire papillary body and the upper portions of the corium were flooded with red blood cells. The smallest capillaries and larger vessels were dilated in most of the sections, but this was not constant. When present the dilated vessels were choked with red blood cells and in some areas a few leukocytes rich in plasma were found in and around the vessels. The

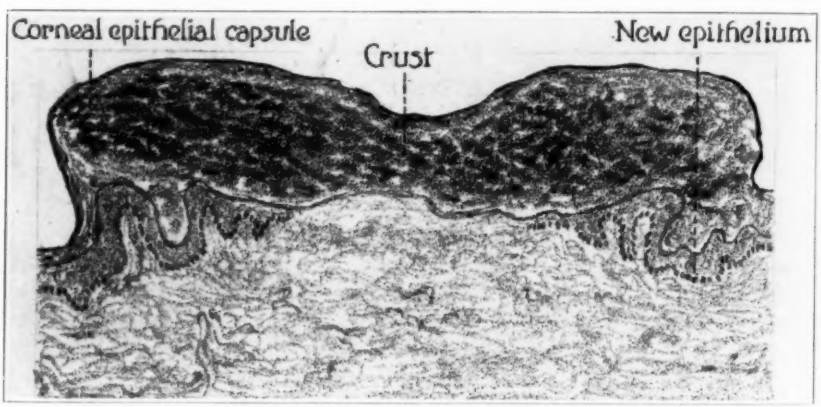

Fig. 19.—Stage 6; crust.

vessel walls were uninjured. In short, the microscopic observations were not characteristic of smallpox unless one found early pocks. The picture was that of severe purpura. The blood observations also were those of purpuric smallpox, showing a low platelet count.

3. *Secondary Purpuric Form.*—Typical smallpox lesions were found in this type, with erysipeloid erythema proceeding to purpura developing later in the course of the disease. Microscopically, the epidermis showed typical vesicular and pustular lesions, and in areas the corium was filled with blood as in the primary type; the blood picture also was the same.

It is difficult to draw a strict line of differentiation between the last two classes, but we believe that the term purpuric smallpox should be reserved for that type in which the purpuric picture predominates.

REPAIR

In all types of advanced smallpox lesions an effort at epithelial repair is found. Almost always a hyperplasia of epithelium at the periphery of all lesions was noted. New epithelial cells pushed inward and downward from the periphery in an apparent effort to heal the surface which had lost its covering.

In cases in which the disease ran its full clinical course the pustular contents gradually solidified and dried, thus converting the pustule into a crust. Before this drying was completed, a shelf of newly formed epithelial cells pushed in from all sides under the crust. The shelf of new cells became cornified on its upper surface so that the crust

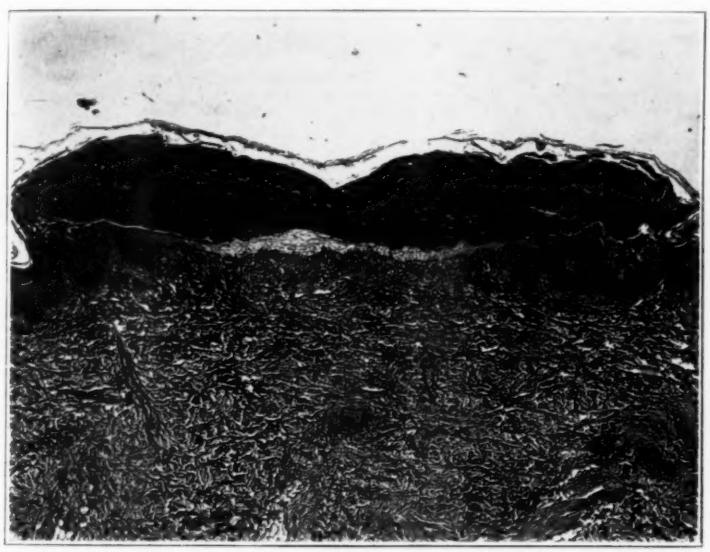

Fig. 20.—Crusting stage showing crust lying within the epithelial capsule.

often lay in a cornified capsule made up of the old dried cornmeal layer above and the newly formed layer below. The capsule was noted particularly in lesions excised from the soles.

The papillae under the crusts were not flattened to any marked extent in our sections, and it is doubtful whether the crusts play an important rôle in scar formation. The crusts were made up of leukocytes, degenerated epithelial cells and tissue detritus. They were almost solid.

SCARS

When the crusts fall off or are removed, depressed and pigmented areas corresponding to the size of the scab remain. It is difficult to state just what determines whether or not a scar will result. When

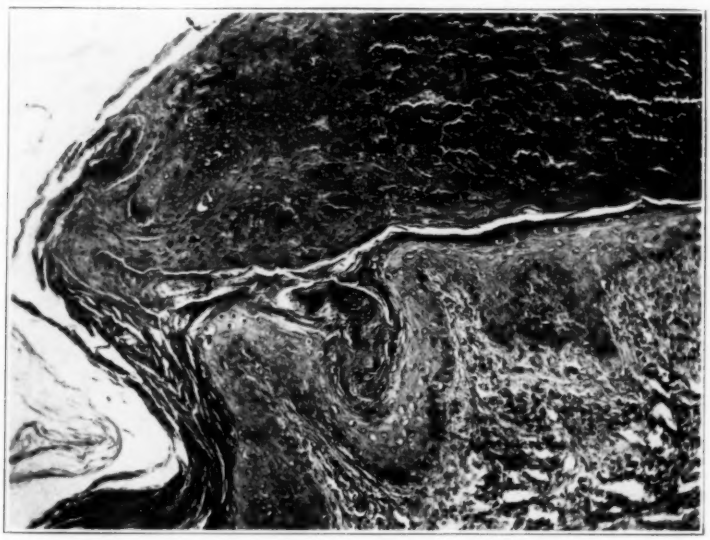

Fig. 21.—Detail of figure 20; new epithelium forming under crust should be noted.

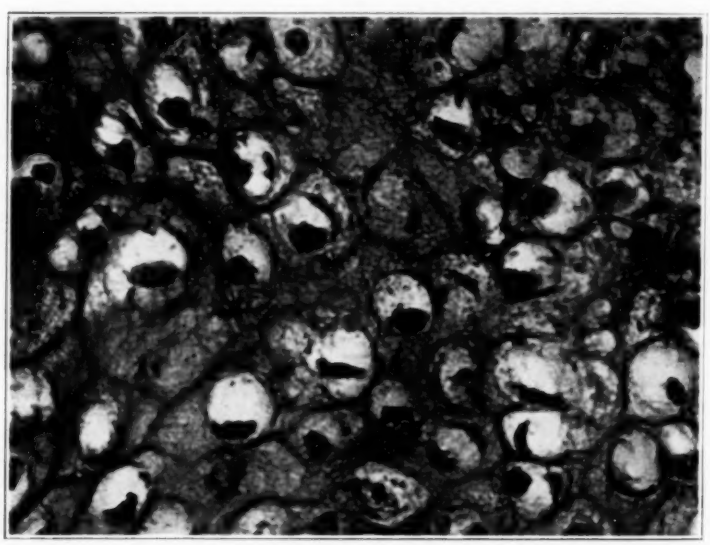

Fig. 22.—High power magnification of details of ballooning degeneration.

scars occur they are usually present only on the face. We examined minutely three patients, one year after they had recovered from severe attacks of variola vera. They said that there were as many lesions on the trunk on a given area as on an equal area on the face; still, no scars were found on the bodies while the faces were badly pitted. The patients said that the crusts were more adherent on the face and dorsum of the hands, and that the spots which bore lesions were livid in color for months after, but that scars resulted only on the face.

We obtained two biopsy specimens from the face, and the microscopic examination showed an atrophic thin epidermis with absence of pegs. The corium apparently was but little altered. With van Gieson's stain the collagen bundles were nearly normal in number and texture. No organized infiltrate was noted. The scar evidently was not composed

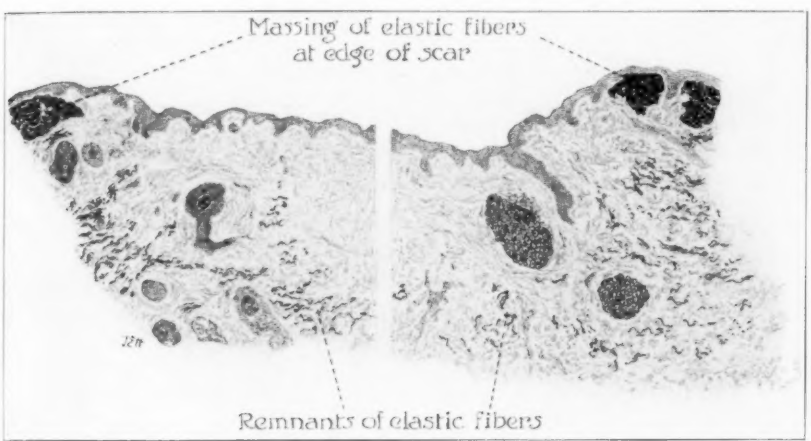

Fig. 23.—Section of variola scar.

of replacement tissue. With elastic tissue staining we discovered a complete loss of fibers in the area of the scar. At the periphery the fibers were dense and thick, appearing as though they had been severed and had retracted to the periphery. This was found in both specimens. We then made elastic tissue stains on one of the early pustules and found the elastic fibers missing in the infiltrated areas. We concluded, therefore, that the smallpox was an atrophic scar in which the epithelium was reduced to a few layers, the corium showing little scar tissue, but a complete loss of elastic fibers.

The mechanism of scar development has been much discussed. Unna did not believe that suppuration alone could cause the destruction of the papillary body. He thought probably prolonged suppuration coupled with inappropriate treatment might cause purulent sequestration, followed by scar formation. Kaposi believed the suppurative

destruction of the papillary bodies caused the scars. Paschen mentioned the possibility of pressure atrophy caused by the encapsulated crust. If this were correct, one would expect deep scars on the palms and soles, but they do not occur. From what we have observed we believe that the virus must have a selective action on the yellow elastic fibers, but we cannot explain why scars only result from facial lesions, unless light rays have some bearing on the mechanism of action. We believe that our observations show the futility of any therapeutic procedure to prevent or alleviate smallpox scarring.

DISCUSSION

Dr. Jay Frank Schamberg, Philadelphia: Dr. Sweitzer has contributed an excellent clinical summary to the knowledge of this disease. From the standpoint of dermatologists a few points might be stressed. One is the great frequency with which patients with syphilis are sent into smallpox hospitals during epidemics of variola. This occurs in all communities, here and abroad. It is well known that syphilis may strongly counterfeit smallpox and at times may confuse competent physicians. There is one diagnostic point to which no reference is made in the literature, and which has helped me in difficult cases. If one or more pustules are present on the palms, the soles, the vermilion border of the lip or the glans penis, there is strong evidence of smallpox rather than of syphilis, for as far as I know syphilitic pustules never occur where there are no hair follicles.

Another cutaneous manifestation is of interest — namely, purpura. Some of you may recall the history of a case published in Flint's Practice of Medicine, in which a medical student, stricken with a severe and curious form of purpura, was visited by many clinicians and students, who likewise attended the autopsy. A number of the students were later attacked by smallpox. In Windsor, Ontario, last year a severe case of "purpura" was the starting point of a bad epidemic of smallpox. Whenever an unusual and severe case of purpura is seen, the question of possible smallpox should be considered.

I believe that the statement made by Councilman many years ago still holds true—that a patient does not die from smallpox per se but from a streptococcic septicemia. This seems to be true even of early hemorrhagic smallpox, as streptococci are recoverable from the blood. If the vesicles of early smallpox are cultured growth is not obtainable on any known medium. On the fourth to the sixth day of the eruption streptococci are found in the lesions and in the blood.

Dr. Richard L. Sutton, Kansas City, Mo.: This demonstration has been valuable. If these pictures could be shown to some of the antivaccinationists, they might be made to see the error of their ways.

Three years ago, in Kansas City, there was a severe epidemic of hemorrhagic smallpox, with a mortality of 82 per cent. The majority of the patients were extremely ill, and of those who died none had been vaccinated within the last twenty years. Many had never been vaccinated.

The eradication of smallpox is purely a prophylactic proposition. There will always be a horde of faddists to combat, but I think progress is being made.

Dr. Charles M. Williams, New York: I wish to emphasize Dr. Schamberg's remarks about the necessity of caution in any case of purpuric eruption.

A man was brought to the hospital on one occasion complaining of severe backache and fever, but exhibiting no other symptoms. Two or three days later I was called at 6 o'clock to see him and found him covered with a hemorrhagic eruption from head to foot. He was dead at 8. There had not been a case of smallpox in New York for twenty years. I think the rapidity of development and the absolute lack of any clue in many cases needs to be emphasized.

Dr. Paul A. O'Leary, Rochester, Minn.: The law for compulsory vaccination has not been in force in Minnesota for several years, but during the recent epidemic of smallpox in Minneapolis and St. Paul, 12,500 persons were vaccinated in a little less than two months, in a town of less than 15,000, so there still seem to be some who have faith in vaccination. In this series there were practically no complications other than an occasional sore arm and a few cases of vaccinia.

Dr. C. Morton Smith, Boston: During the epidemic of smallpox in 1901 and 1902, I saw a case of erythema caused by copaiba which closely resembled hemorrhagic smallpox. I think it is well to bear in mind that some of the drug eruptions may simulate closely certain types of smallpox.

Dr. Harry E. Alderson, San Francisco: California is exposed to smallpox from Mexico and the Orient, and the preventive measure are opposed by the Christian scientists and other cultists who are numerous in California, particularly in the southern part of the state. Recently a patient came in on one of the Pacific liners in whose case a diagnosis of purpura hemorrhagica was made. The patient died of smallpox in a San Francisco hospital. Nineteen cases were traced to that one, and the mortality was high. A nurse and some attendants at the hospital died, and also some employees at the undertaking establishment where the body was taken. The epidemic in California is subsiding now. In 1925 there was an epidemic, but the mortality was only 0.5 per cent. During the first five months of this year the smallpox mortality in California has been 9 per cent. Many cases are of the hemorrhagic type. Recently I had a case in a woman who was pregnant, at about full term, and I was called in when the eruption was in the pustular stage. For several days she had been taken care of by a Christian scientist, who went into the house and left at will. It was necessary to have a consultation because the Christian scientist objected to the diagnosis, and the patient and family refused to be vaccinated. Dr. Culver and Dr. H. J. Templeton were called in consultation, and we finally convinced the people that smallpox existed. The patient went into labor with the pustular eruption present. A perfectly healthy infant was delivered, and it was vaccinated on the second day. The vaccination was successful, and there was no trouble after that.

Dr. William Allen Pusey, Chicago: There are two things which I wish to point out. First, the opinion is developing that the way to get dermatologic research work done in dermatology and in other specialties is to have it done by men who are primarily research workers who are not particularly skilled in clinical work. In dermatology, at least, discoveries are made by dermatologists. Research workers have been useful helpers, but they have neither led nor pointed the way. A good illustration of this fact is seen in the papers read by Drs. Sweitzer and Michelson.

Another point was brought to my mind by Dr. Alderson's remarks. He said that California was exposed to smallpox because of its proximity to Mexico. I should qualify that by saying that those California people who

are not willing to be vaccinated are exposed to smallpox. It seems to me that it is the physician's business to give the people information as to how they can protect themselves and then to leave it to them whether they carry it out or not. I think it is rather futile for us, or any other group, to try to act as guardians of the world. People should accept their own responsibilities. Physicians should resist the efforts of cultists to interfere with the advancement of the knowledge of the medical sciences.

Dr. George D. Culver, San Francisco: I am always interested in smallpox for I had it twenty-seven years ago. In 1907 there was a small epidemic in San Francisco, and I think I saw all of the cases. During that time there was only one death, and in that case there was the complication of pneumonia.

In reference to the scarring, I have two scars on my left palm from smallpox pustules. I have several on my face, one on my left lower eyelid which is something of a bother.

I saw the pregnant woman mentioned by Dr. Alderson. After I saw the patient, her mother, a cult follower, went with me into the bathroom while I was washing my hands, and said, "My daughter has nothing the matter with her. I cannot see a thing." I told her that did not matter, that I had to think of the baby, and that her daughter must be treated accordingly.

Dr. Harold N. Cole, Cleveland: The association is not only for our own benefit but also for the benefit of the public, and I think it would not be a bad plan for it to go on record, perhaps to be broadcast through the *Journal of the American Medical Association,* with a resolution as to the severity of the variola of today. I would also like to emphasize the difficulty in making a diagnosis in the hemorrhagic types of the disease, especially in the sporadic cases. In these cases I use the Powell test and find it of great value.

Dr. A. M. H. Gray, London: I think probably there is a much larger population of unvaccinated people in England than there is in this country, and I cannot share the optimism of Dr. Sutton that showing these pictures to antivaccinationists would have any influence on their intelligence. I think that there would be no gain in demonstrating the effect of the disease. I agree entirely with Dr. Cole as to the advantages of the medical profession propagating information for the benefit of those who know nothing of the disease. The propaganda of the antivaccinationists is extremely vicious, and physicians should try to counteract it. In my country there is a society which carries out active propaganda, and there is not the slightest question but that it has a great effect in counteracting the propaganda of the antivaccinationists. At the same time there is a question whether the best results are obtained by propaganda or by force. In my country, however, I think better results are obtained by propaganda.

In the last picture Dr. Michelson showed of the scarring in smallpox, there was a bundle of elastic tissue on each side of the scar. Were these bundles visible to the naked eye, and are they always at the edge of the scar and never in the center? In certain conditions this elastic tissue appears at the center of the scar, and I think the paper of With and Kissmeyer of Copenhagen, who wrote exhaustively on these conditions, will be remembered.

Dr. Sigmund Pollitzer, New York: I was particularly interested in this presentation because this is the twenty-fifth anniversary of a paper on the same subject, with lantern slides, which I presented at the Chicago meeting of the association in 1901, based on the outbreak of smallpox in New York in 1899 and 1900. As a diagnostician in the health department at that time I had an opportunity to see nearly all of the cases, about 1,000 altogether. Nothing

has been added to our knowledge of smallpox clinically in the last twenty-five years. The disease was better and certainly more widely known a hundred years ago than it is today. Few physicians today have an opportunity to see smallpox.

In regard to the hemorrhagic cases, it should be borne in mind that there is a hemorrhagic smallpox which does not look like smallpox. If this is kept in mind, occasionally a case may be seen. If an epidemic were going on one would think of it, but often an epidemic is ushered in with tremendously severe cases which no one recognizes until something like an epidemic has occurred.

Little has been added to our knowledge of the histology and the pathologic anatomy of smallpox during the last twenty-five years. The work of Councilman and his associates in 1902 summed up the knowledge thoroughly. The value of such papers as the one today lies in their calling attention to the fact that there is such a thing as smallpox.

I believe there should be strict legal enforcement of vaccination. I know that meets with opposition on the part of many people, but so do legal exactions against all forms of quackery. There are those who carry their idea of personal liberty so far that they think that people should be allowed to die of smallpox if they wish, or that they should be allowed to pray over syphilis if they wish. The state justly assumes the right to regulate matters of health, and it is well to say "You shall not have smallpox," as smallpox always entails a great economic loss to the community. That vaccination does not invariably protect is well known, but the fact that it does protect in the great preponderance of cases should make it obligatory. It is known that even smallpox itself does not protect in all instances. I saw a case in a man who had had smallpox twenty years before. This diagnosis was based on his statement that he had had smallpox, and had been in the pest-house in St. Paul at that time. Cases of this kind are extremely rare, as are cases of smallpox after vaccination. I still have my collection of slides of smallpox that I showed twenty-five years ago, and I remember one histologic section of varicella. I think the contrast of the two types of vesiculation is interesting.

Dr. Charles M. Williams, New York: The cases of hemorrhagic smallpox occurred in 1899, just at the beginning of the epidemic to which Dr. Pollitzer refers.

Dr. Samuel E. Sweitzer, Minneapolis: In the differentiation from syphilis confusion often arises. I had a patient with pustular syphilis who had been confined for fifty-two days in a pest-house in a neighboring state.

Dr. Sutton misinterpreted the figures regarding the mortality rate. The hemorrhagic pustular cases had a fatality of 79 per cent, and the purpuric cases 100 per cent. In the purpuric cases that did not show any pustulation we depended on the blood examination. We were so rushed we did not have time for the eye test. None of the patients died who had been vaccinated within seven years.

I do not agree with Dr. Pusey, for several reasons. I think vaccination should be compulsory. At times of epidemics the power is given to enforce the law by going to schools and such places and carrying out vaccination, but the public, unfortunately, does not average high in intelligence. The public depend on the health authorities, and they would ask, "Why do you not enforce vaccination?" They know nothing about it. There should be a rule enforcing vaccination at school age, at least, and that would prevent most of the cases.

I would like to tell Dr. Gray that after several of the Christian scientists in our community died, the rest decided to be vaccinated, or at least several of them did. One or two died, and then there was a rush to be vaccinated. It does not take much to change their point of view.

We had several mild cases of varioloid in patients who had been protected by vaccination several years before.

Dr. Henry E. Michelson, Minneapolis: In regard to the epithelial giant cells found in varicella, I would refer Dr. Gilcrist to a recent, very complete article by Hammerschmidt.

I cannot answer Dr. Gray's question about the scarring. To any one interested I would like to mention a comprehensive pamphlet that the Royal Research Society of England has recently published on smallpox.

A SYNDROME OF BLENNORRHAGIC KERATODERMA

REPORT OF A CASE *

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Blennorrhagic keratoderma is still sufficiently rare to justify the report of a case, only sixty-five cases being recorded in the literature to date. The present case possesses some novel clinical features lending additional interest.

REPORT OF CASE

H. L., aged 28, unmarried, an exmedical student and an advertising solicitor, was admitted to the Los Angeles General Hospital on June 23, 1924, complaining of intense pains in several joints, general weakness and peculiar skin lesions. The family history was not important. The patient had had almost all the infections of childhood. He had been well from childhood until 1911, when he had had inflammatory rheumatism in the left knee for two weeks. During the last few years, he had suffered from asthma. Eight years before, he had had a severe attack of gonorrhea, which had lasted for sixteen months. At that time there had not been any joint or skin trouble. Six months before admission, after a venereal exposure, he had had a purulent discharge from the urethra for one day. Two weeks later, the joints began to swell and become painful. First the joint of the left knee was affected, next, the shoulder joint and then the left ankle, right ankle, right knee and right elbow joints. Two weeks later, the skin lesions began to appear as "boils and pimples," which were breaking down, exuding a discharge and drying up into crusts.

Physical Examination.—The patient was a man of average height and slender build. He was extremely pale and bore an expression of acute suffering, weakness and toxemia. The joints mentioned above were considerably enlarged, inflamed and excruciatingly painful. In fact, the pain was one of the most striking features of the case. The patient could not attempt the slightest motion of his lower limbs without producing agonizing pains. The small interdigital joints on both feet appeared to be swollen, inflamed and painful to touch.

Examination of the head, chest and abdomen did not reveal any pathologic changes. There was no urethral discharge. Clinical evidence of gonorrhea was not obtained by examination of the prostate and seminal vesicles. There was a purulent discharge and evidence of an abscess in the perineum. A rectal examination was attempted but had to be abandoned because of extreme pain.

Skin Observations.—The skin observations presented a unique and most spectacular picture. Four types of skin lesions were seen. Many small, crusted papules and pustules, dark red and soft, were scattered irregularly on the trunk, limbs, scrotum and penis. Fifty or sixty discrete, oval and round lesions, ranging in size from that of a coffee bean to that of a finger nail, which were inflammatory, crusty and not itchy, were scattered irregularly on the trunk and limbs. There were four or five conical, discrete, papular formations, shaped like an inverted funnel, the size of a small acorn. These lesions were semisolid, horny, homogenous and translucent, ranging in height from 0.5 to 1 cm., and they

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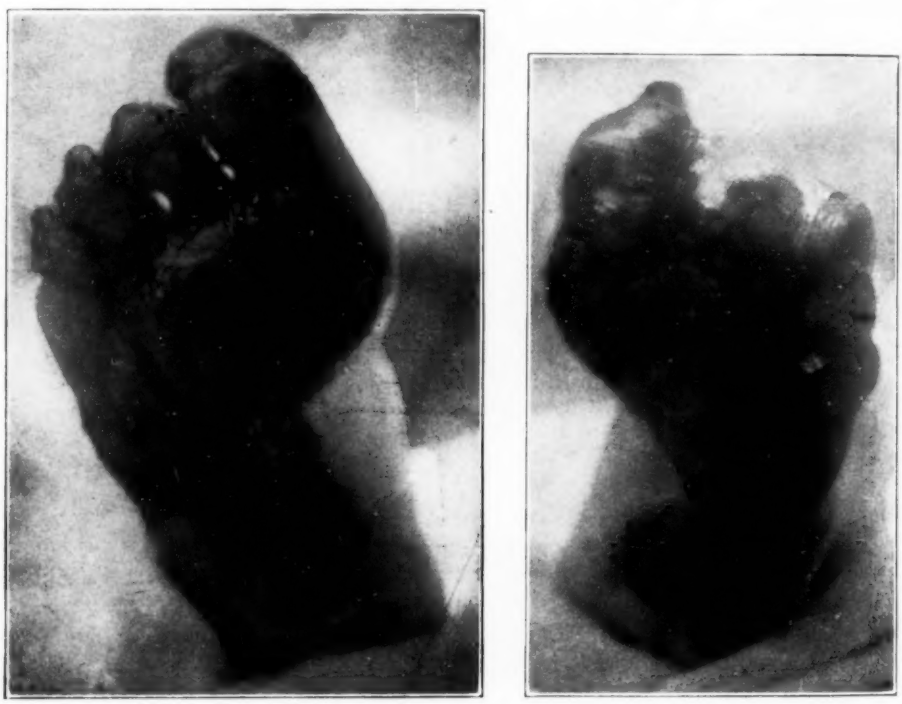
conveyed a perfect impression of cutaneous horns. All the lesions could easily be scooped out as a whole with a sharp instrument, leaving a soft dark base, identical with that of the previously described crusted, psoriasis-like lesions. The most striking and spectacular lesions were found on the soles. The affected area corresponded exactly to the imprint area of the sole. The lesions were symmetrical and presented a number of discrete, elevated, dark red, black and brown patches, which ran together and coalesced into large, geographic, maplike areas. The central part of the patches was made up of horny deposits and the periphery presented a dark red, inflammatory, soft base. However, a number of similar patches still remained discrete at the periphery of the main area. The lesions



Lesions of blennorrhagic keratoderma on patient's feet.

presented thick deposits of soft, boggy, homogenous, horny, yellowish, leather-like, semitranslucent tissue, ranging in depth from 0.75 mm. to more than 1.5 cm. The maximum height of these deposits was reached on the toes, particularly on the big toes.

The whole affected area of the soles, particularly the joints, was so extremely painful that the patient shrank from the slightest touch. It may be of interest to note that the patient, an intelligent man, persistently complained of a "sloppy" feeling in the feet, such as one has when walking in the rain wearing leaky shoes.

Laboratory Observations. The blood pressure was 110 systolic and 64 diastolic. The Wassermann reaction was negative. Examination revealed: blood sugar, 125 mg. per hundred cubic centimeters of blood; urine, specific gravity 1.018; no sugar and albumin; total nonprotein nitrogen, 30 mg.; preformed creatinin,

1.3; uric acid, 4. A blood culture gave negative results. A gonorrheal complement-fixation test was requested, but the pathologist did not have any faith in its value. A roentgenogram of the left knee joint did not show any material pathologic condition.

Course and Treatment.—Before entering the hospital the patient was given a few staphylococcus injections, without any apparent effect on the local or general condition. In the hospital a course of gonorrheal vaccine injections was given. The initial dose of 1 cc. was too strong and gave considerable reaction. The dose was reduced to 0.5 cc., which was given every three or four days. This dosage was well tolerated. The patient began to improve slowly but steadily. The temperature during the entire course was subacute, ranging from 99.2 to 100.2 F. and gradually returning to normal. There was a temporary setback only once, and this occurred shortly after the 1 cc. injections of vaccine were started. Several of the affected joints showed exacerbation and became more painful. Most peculiar skin lesions developed simultaneously on the palmar surface of the distal phalanx of all fingers, extending to the finger-nails. These were yellowish, homogenous, waxy, solid, longitudinal masses, the deposits in appearance suggesting leather strips.

The local treatment was of a symptomatic nature, such as bathing the feet with a hot permanganate solution and a mild salicylic ointment. The lesions on the rest of the body did not receive local treatment. The skin lesions gradually peeled off and disappeared, leaving no scars, but slight pigmentation.

The patient improved steadily, and on Aug. 27, 1924, left the hospital, being able to walk. Six months later, he had fully recovered from the attack, had regained complete mobility of the joints and did not present any marks of the skin lesions.

Diagnosis.—The striking syndrome of a gonorrheal attack in the past, of the peculiar multiform, keratotic, plantar and palmar lesions and of multiple, severely painful, subacute inflammatory arthritides, and the presence of marked toxemia, strongly suggested the diagnosis of blennorrhagic keratoderma.

Morphologically, the patches and the platelike lesions on the soles were so unusal and fitted so perfectly the picture of the "relief maps," emphasized in the literature on blennorhagic keratoderma, that only this diagnosis was considered.

PATHOLOGIC CONDITION

Biopsy was refused and was not insisted on because the microscopic changes of blennorrhagic keratoderma are not pathognomonic, and its diagnosis can be established more conclusively when based on the morphologic and clinical study of a case.

One fact of interest should be emphasized from the pathologic point of view. All writers studying the microscopic changes of blennorrhagic keratoderma seem to agree that parakeratosis, rather keratosis, is the main and predominant microscopic feature. However, it has not been brought out, as it should be, that blennorrhagic keratoderma is one of the few, if not the only, dermatoses in which parakeratosis is also the predominant gross pathologic clinical feature. I know of no other dermatosis in which one sees such massive parakeratotic deposits and formations which remain in this half-formative stage and do not reach

the final dry and hard stage of cornification. It is true that in a few reported cases "horny carapace" plates were described, but even in these cases the bulk of the eruption retained the gross clinical appearance of waxy, soft, homogenous, parakeratotic deposits. For this reason I heartily endorse the claim of such observers as Haase,[1] Stillians [2] and others who urge that the correct name should be blennorrhagic parakeratosis rather than keratosis.

BLENNORRHAGIC KERATODERMA VS. ARTHROPATHIC PSORIASIS

Adamson [3] and a few other authors stated that it is hard to differentiate blennorrhagic keratoderma from arthropathic psoriasis. I cannot subscribe to this statement. I can still less accept the extreme view expounded by Falk,[4] who denies altogether the blennorrhagic keratoderma as an independent clinical entity and includes it in the group of atypical cases of arthropathic psoriasis.

The lesions that give rise to the confusion are round or oval crusted patches on the trunk and limbs observed in many cases of blennorrhagic keratoderma. Such lesions were also present in the case reported. However, a closer morphologic study of individual lesions readily refuted the idea of the resemblance to psoriasis conveyed by the general impression. The lesions were soft and at times presented hill-like conical elevations not seen in psoriasis. The scales were yellowish, soft, friable and glued together sufficiently to be called crusts rather than scales. What is more important—as a differential feature—some of these lesions, simulating perfectly cutaneous horns, could be shelled out as a whole by a sharp instrument, leaving a smooth, dark red, inflammatory base. The homogenous, yellowish, keratotic plates, like gigantic relief maps, on the soles were so unlike anything seen in any type of psoriasis as hardly to require differentiation.

Besides the morphologic differences cited, the whole clinical syndrome and the clinical evolution of the lesions are entirely different from those of arthropathic psoriasis. Arthropathic psoriasis is essentially a chronic condition and does not affect the general nutrition; the arthritic changes are characteristically sluggish and painless and are of the degenerative structural type of arthritis deformans.

Blennorrhagic keratoderma, on the other hand, is a toxic, inflammatory process which runs a febrile course and is accompanied or preceded by a gonorrheal attack, which profoundly affects the general

1. Haase: J. Cutan. Dis. **34**:817 (Dec.) 1916.

2. Stillians, A. W., and Zeisler, E. P.: Gonorrheal Keratoderma, Arch. Dermat. & Syph. **8**:393 (Sept.) 1923.

3. Adamson: Brit. J. Dermat. & Syph. **32**:183 (June) 1920.

4. Falk: Arch. f. Dermat. u. Syph. **129**:299, 1921.

nutrition and may bring about the gravest toxemia and anemia. The arthritic leisons are of acute inflammatory nature and are extremely painful.

The mere fact that blennorrhagic keratoderma and arthropathic psoriasis have one microscopic feature of parakeratosis in common should not give rise to confusion and difficulty of differentiation, much less justify the consideration of the two conditions as identical. There are many other dermatoses presenting a microscopic picture of parakeratosis, such as seborrheic dermatosis, pityriasis rubra pilaris and exfoliating dermatitis—yet no one would assert that they are related to or identical with blennorrhagic keratoderma, as their clinical and morphologic characteristics are entirely different.

COMMENT

In spite of the fact that the clinical type of the skin lesions is so clear-cut as to render morphologic diagnosis of blennorrhagic keratoderma unassailable, the final diagnosis is still held in abeyance, because an important link of etiologic relationship with gonorrhea could not be found. Unexpectedly, the examination of the genito-urinary tract has failed to reveal clinical evidence of gonorrheal infection. The perineal abscess, obviously, could not bear an etiologic relationship to the syndrome described, because it appeared after the skin and joint lesions were fully developed.

In view of these observations, the case permits of a double interpretation. It may be one of those cases of blennorrhagic keratoderma in which the gonorrheal infection preceded by a long period the outbreak of the skin and joint lesions. Such cases are found in the literature. Thus, in a case reported by Graham Little,[5] gonorrhea was present twenty years before the skin and joint lesions. Little cites Williams' case in which urethritis was present thirteen years before. Doble, in 1921, reported a case in which gonorrhea preceded the other conditions by four years. Adamson and Hallopeau reported similar cases.

Such long periods of latent infection are not impossible of explanation because blennorrhagic keratoses are assumed by practically all observers to be of toxic and not of bacillary origin.

The prompt response and steady improvement in this case from gonorrheal vaccine seems to be of considerable confirmatory diagnostic importance, as the curative value of gonorrheal vaccine in these cases is emphasized by many observers. It is to be regretted greatly that, for accidental reasons, the complement-fixation test has not been utilized.

That the cure obtained in this case from a gonorrheal vaccine was due to its specific action and not to a nonspecific immunization of the

5. Little, Graham: Practitioner **97**:531 (Dec.) 1916.

foreign protein, can be deduced from the fact that mixed staphylococcic vaccines were used previously without effect.

Of great interest and possibly of considerable diagnostic significance should be mentioned the intense focal reaction observed after the first 1 cc. dose of gonorrheal vaccine. These injections not only increased the general malaise, fever and arthritic symptoms, but also brought out on the palmar surface of the fingers peculiar, yellowish, homogenous keratotic deposits, identical in character with those on the feet.

This unintentional experimental reproduction of the original lesions conveys a strong confirmatory suggestion of the gonorrheal nature of the eruption.

Serologically, the phenomenon resembled the Herxheimer reaction in syphilis, with the difference that in this case the source of the specific toxins was ectogenous in the form of gonorrheal vaccine, while in the Herxheimer phenomenon the source of toxins is endogenous, the toxins being liberated by the spirocheticidal action of arsenicals.

The second interpretation of the case would be that the syndrome of blennorrhagic keratoderma, comprising the characteristic skin lesions, arthritis, and other features, were induced, not by gonorrhea, but by some other infection preceding the onset of the acute attack and overlooked by the patient and the medical attendant. If this interpretation is correct, this case would be the first reported instance of the syndrome of blennorrhagic keratoderma induced by some other type of infection than gonorrhea. This gives rise to the interesting question whether blennorrhagic keratoderma is a definite clinical entity or merely a syndrome which may be caused by various types of infection.

SUMMARY

A case is reported presenting a typical clinical picture and a typical course of blennorrhagic keratoderma. In view of the absence of active gonorrhea, it is doubtful whether blennorrhagic keratoderma is a definite clinical entity or merely a syndrome.

MONILIA INFECTION OF THE TONGUE*

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Since Robin in 1853 named the thrush fungus *Oidium albicans,* there has been a continuous controversy as to the botanic position of this parasite. The chief ground for dispute appears to be the fact that growth on some artificial mediums takes place as a yeastlike form and on others as long branching mycelia similar to the morphology of the molds. Recent workers have shown by more accurate measures that ascospores are absent, and by utilizing fermentation tests, agglutination reactions and experimental inoculations, have demonstrated that the thrush parasite should not be included among the oidia or saccharomyces, but that it belongs to the monilia family (Hansen, Reess and others). The term *Monilia,* as understood today by mycologists, has been extended chiefly by the researches of Castellani and Pinoy to include every yeastlike organism which forms mycelia, even in small amounts, but no ascospores on certain mediums. For practical purposes, Castellani uses the following classification of the yeastlike fungi: (*a*) asci present—(1) mycelium absent = *Saccharomyces;* (2) mycelium present = *Endomyces;* (*b*) asci absent—(1) mycelium absent = *Cryptococcus;* (2) mycelium present = *Monilia. Oidia* are characterized by the absence of budding forms, and the presence of arthrospores and well developed mycelia.

REVIEW OF LITERATURE

The investigations of Castellani [1] on the *Monilia* group merit special consideration. He has isolated a large number of strains of *Monilia* in tropical as well as temperate climates from such conditions as bronchomycosis, sprue, thrush and dermatomycosis, and from vaginal discharge. Immunization phenomena and biochemical properties are considered of greater importance in differentiation than pure morphology. The genus *Monilia* is characterized by septate mycelia with fertile hyphae often bearing at their extremities short chains of rather large oval conidia. It grows best on Sabouraud's maltose agar or dextrose agar, better on slightly acid mediums under two types, the yeastlike and the filamentous. The biologic reactions with milk, gelatin and sugar mediums vary. Rabbits can be immunized and agglutination reactions used for differentiation. Castellani has demonstrated that the well-known clinical condition of thrush, occurring as white patches on the buccal mucosa chiefly in

* Read at the Golden Anniversary Meeting of the American Dermatological Association, Philadelphia, May, 1926.

1. Castellani and Chalmers: Manual of Tropical Medicine, 1919, p. 108.

nursing infants, may be due to several different fungi, such as *Monilia albicans, Monilia candida, Endomyces vuillemini, Monilia tropicalis,* etc. He emphasizes the fact that the term thrush fungus has been used in the past to cover a number of different species, and he reserves the term *Monilia albicans* for the species which clots milk and liquefies gelatin. *Monilia candida* is characterized by a thinner mycelium and rounder conidia. It has been found in a few cases of bronchomycosis and may produce white patches on the tongue and buccal mucosa similar to those in thrush. Engman and Weiss [2] have reported an unusual instance of *Monilia candida* infection of the mouth secondary to a carcinoma of the tongue. Recently, Castellani [3] and Sergio Re [4] have reported finding a hitherto undescribed yeastlike organism, *Monilia macroglossiae,* in several peculiar cases of blastomycetic macroglossia. Clinically, the whole tongue was enlarged and painful, producing discomfort in eating; but no verruccoid patches were seen as in blastomycosis. From deep scrapings, a yeastlike, gram-positive oval fungus was isolated which was agglutinated by the patient's blood in 1:4000 dilution. Asci were never observed, but mycelial production was not rarely visible in liquid mediums. There was no gas production on any sugar mediums which would place the lesion in the zeylanica type.

Recent investigations appear to attach greater importance to the pathogenic possibilities of yeastlike organisms isolated from mouth, throat and cutaneous conditions. The frequency with which yeasts are reported in throat cultures, and their presence in swabs from sore throats suggests that yeasts may be normal inhabitants of the mucous membranes, and that they may be saprophytic as well as pathogenic. Among early investigators who isolated yeasts from the throat may be mentioned Troisier and Achalme, de Stöcklein and Foulerton.[5] Wilson [5] found yeastlike organisms in 136 cases of respiratory infection characterized by a membrane in the throat, which were negative for diphtheria. Grover [5] states that yeasts are present in a certain percentage of normal throats. Tanner and Dack [6] have made a careful study of twenty-two strains of yeastlike fungi collected from throat swabs. They possessed characteristics which probably classed them with the thrush fungi, and

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2. Engman, M. F., and Weiss, R. S.: Monilia Candida Infection of the Mouth, Arch. Dermat. & Syph. **1**:119 (Feb.) 1920.

3. Castellani: Notes on Three New Yeast-Like Organisms and a New Bacillus, with Remarks on the Clinical Conditions from Which They Have Been Isolated: Furunculosis Blastomycetica, Macroglossia Blastomycetica, Stomatitis Cryptococco-Bacillaris, J. Trop. Med. **28**:217, 1925.

4. Sergio Re: Observations on the Cultural and Biochemical Characters of Monilia Castellani and Monilia Macroglossiae, J. Trop. Med. **28**:317, 1925.

5. Foulerton, Wilson and Grover, quoted by Tanner and Dack (footnote 6).

6. Tanner and Dack: A Study of Yeasts from Sore Throats, Centralbl. f. Bakteriol. **91**:283, 1924.

since ascospores were not found they were probably *Monilia*. Inoculation experiments with white mice, guinea-pigs and rabbits indicated that all but one strain possessed pathogenic properties. Subcutaneous and intraperitoneal injections were least harmful. Death followed intravenous injection in rabbits in a short time. Intraperitoneal injection into white mice also terminated fatally. Nonpathogenic yeast prepared for injection in the same manner caused no symptoms of illness, and, with one exception, seemed to be harmless. Agglutinins were found in rabbits and the yeasts were probably destroyed by phagocytosis.

Peckham,[7] working along similar lines of investigation, has isolated fifty-one cultures of yeasts from human sources, twenty-five from the throat, nineteen from infant's mouths, six from sputum and one from the vagina. Forty-five of these were identified as *Monilia*, of which thirty-eight were pathogenic; five were classed as *Oidia* and one as *Saccharomyces*. Guinea-pigs were used for injection, and the yeasts were recovered in pure culture from abscesses in the groin. They were also found after death in the pancreas, liver, spleen and omentum. One typical yeast was studied carefully and it was found that its injection into animals produced a lymphopenia, induced the formation of antibodies, was toxic in the systemic effects and produced localized lesions characterized by necrosis and infiltration of endothelial cells fusing to form giant cells. A glycosuria was produced by obliteration of the islands of Langerhans in the pancreas. The effect of the yeasts on the blood and tissues of animals suggests that they may be additional factors in infections caused primarily by other organisms.

Ashford,[8] in numerous publications, has sought to establish a special genus of monilia—*Monilia psilosis*—isolated from the tongue and stools as the specific cause of sprue, a tropical form of diarrhea. In his most recent article, Ashford [8] states that he conceives sprue in the tropics to be a congener of thrush in the north, as *Monilia psilosis* is a congener of *Monilia albicans*. Both are distinct clinical entities and are usually infections based on a state of nutritional imbalance—in the case of sprue on a condition of chronic digestive incompetence; in the case of thrush, on the marasmus of infants, of the senile and of subjects wasted by chronic disease. At times, without the previous state of malnutrition, both may be produced by sheer force of infection. Recently, however, Wood [9] has isolated *Monilia* indistinguishable from the psilosis variety from the tongue scrapings and stools in cases of pernicious anemia.

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7. Peckham: Study of Yeasts from Human Sources, J. Infect. Dis. **37**:53, 1925.

8. Ashford and Hernandez: Blood-Serum Calcium in Sprue and Other Pathologic States in the Tropics, Am. J. M. Sc. **171**:575, 1926.

9. Wood: Further Study of Possible Relationship of Monilia Psilosis to Sprue and Pernicious Anemia, South. M. J. **87**:519, 1925.

Other writers, such as Manson, Bohn and Dold, also do not accept Ashford's conclusions. Hines,[10] using a classification based on agglutination reactions, found no absolute degree of specificity between sprue yeasts, wild yeasts and blastomycetes. He contends that the cultural and morphologic criteria set up by Ashford (inverted pine-tree growth in gelatin, gas formation with maltose, dextrose and levulose, nonfermentation of inulin and death in twenty-four hours on intravenous injection into rabbits) are not sufficiently distinctive to identify *Monilia psilosis* from other species of *Monilia*.

In recent dermatologic literature, the occurrence of yeastlike fungi is being reported from a large variety of cutaneous lesions. Shelmire [11] has published an excellent summary of this subject with a review of the pertinent literature. Under the heading of thrush infection of the skin, he includes the cutaneous conditions reported by other observers as due to *Oidia, Endomyces, Saccharomyces,* yeasts, "Spross-pilze" or "Soorpilze." Among the mycoses described are the disseminated lesions seen over large areas of the skin after waterbed treatment, after wet dressings and in nursing infants; furthermore, the intertriginous infections around the anus, genitals, under the breasts and in the axillary and interdigital folds. The so-called erosio interdigitalis blastomycetica and a group of chronic paronychias are also referred to thrush infection. Shelmire stresses the fact that for a diagnosis it is necessary to find in scrapings and smears the mycelial threads and groups of spores in cluster-like arrangement. The mycelia are long, thin and mostly unseptate, and they exhibit little branching and show short lateral and side budding. Growth on maltose-agar is profuse, young colonies appearing as a pure yeastlike growth of round or ovoid cells and older cultures showing single and branched mycelia with side budding and clusters of spores, either free or attached to the mycelia. In this connection, attention should be called to Jessner and Kleiner's [12] observation. In 59 per cent of 150 patients saprophytic yeasts grew apparently from the scrapings of normal nails. By scarification and maceration of the interdigital spaces erosive lesions were produced in a large proportion of cases.

Fleisher and Wachowiak,[13] in a preliminary report, have found *Monilia* or monilia-like organisms in the feces of 82 per cent of thirty patients with psoriasis, in the blood in 21 per cent and in skin scrapings

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10. Hines: Studies on the Identification of Monilia Psilosis, J. Infect. Dis. **36**:529, 1924.

11. Shelmire, Bedford: Thrush Infections of the Skin, Arch. Dermat. & Syph. **12**:789 (Dec.) 1925.

12. Jessner and Kleiner: Über das Vorkommen von Sprosspilzen an Normalen Nägeln und ihre Pathogenität, Arch. f. Dermat. u. Syph. **149**:363, 1925.

13. Fleisher, M. S., and Wachowiak, M.: Monilia as Possible Etiologic Factor in Psoriasis, Arch. Derm. & Syph. **11**:756 (June) 1925.

in 16 per cent. In normal persons, *Monilia* was found in only 6 per cent of 100 stools; this organism was not found in the skin of the body or in blood cultures in any case. Their results suggest that *Monilia* or similar organisms may have some causal relation to psoriasis. These observations need further confirmation.

The foregoing review of the literature warrants the conclusion that yeastlike organisms are found in a wide variety of conditions of the mucous membrane and of the skin, and that, first, the presence of *Monilia* may indicate a primary condition in which *Monilia* is the actual causative agent; second, they may act as secondary invaders, and, finally, they may exist as saprophytes without any pathogenic action. Castellani states that the pathogenic varieties isolated from the mouth belong generally to the types *krusei, pinoyi, metalondinensis* or *tropicalis*. My own interest in this subject has been stimulated by the isolation of two strains of yeastlike organisms from two cases presenting unusual lesions—on the tongue in one case and on the tongue and lips in the other.

REPORT OF CASES

CASE 1.—*Monilia pinoyi infection of the tongue in association with polycythemia vera and chronic arteriosclerotic myocarditis.*

History.—Mrs. Z., aged 56, entered the medical service of Michael Reese Hospital on March 19, 1925.[14] Her principal complaint was headache and swelling of the feet of recent date. This was preceded for several years by shortness of breath and precordial pain. In addition, she had occasional attacks of vomiting, abdominal distention and constipation. She could not recall how long the condition of the tongue had been present, and she did not suffer any discomfort from it.

Physical Examination.—The patient had the appearance of a chronic, undernourished invalid, with markedly flushed though sunken cheeks. The pupils were irregular but reacted to light. There was slight nystagmus. The face and lips were markedly cyanosed and the ankles edematous. The spleen was large and firm, not tender. The liver was palpable one hand's breadth below the costal border, smooth and somewhat tender. There was marked diastasis of the recti muscles and visible peristalsis. A soft systolic murmur was heard at the base and apex of the heart. Scattered râles were heard throughout the lungs and dulness and diminution of breath sounds at the bases. There was no pathologic condition of the pelvis. Eyeground examination showed both disks redder than normal, the veins overfilled and rigidity of the arterial walls, suggesting arteriosclerotic changes. The diagnosis of the medical condition based on the cyanosis, enlarged spleen and liver and blood observations was a polycythemia vera, with generalized arteriosclerotic changes, chronic myocarditis and advanced failure of the heart.

Condition of the Tongue.—The tongue as a whole was slightly enlarged and covered with a peculiar exanthem. Over the dorsum and sides of the tongue were narrow branching and arborizing white lines or streaks, slightly raised above the surface and adherent, producing a striking geographic appearance. There was no rapid shifting and disappearance of the lesions as is usually seen

14. Permission for reporting this case was granted by Dr. W. W. Hamburger.

in the so-called wandering rash or glossitis areata exfoliativa. Only after several months' observation, when the patient's general condition had improved, was there a lessening of the exanthem. The rest of the mouth was free from evidence of disease. The tonsils were flat and submerged. The clinical diagnosis was a mycosis of the tongue. Syphilis, tuberculosis and other pathologic conditions could be ruled out clinically.

Laboratory Observations.—The blood observations on admission were hemoglobin content, 100 per cent plus; red blood cells, 9,760,000; white blood cells, 16,000. Abnormal nucleated forms were not found, but a few microcytes and macrocytes were present. The platelets appeared to be normal in number but unusually large. A subsequent blood count showed: red blood cells, 8,200,000; leukocytes, 11,100. The Wassermann reaction was negative. The systolic blood

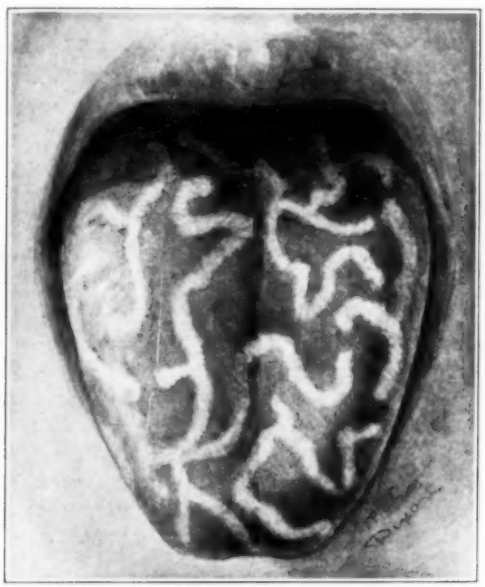

Fig. 1 (case 1).—Monilia pinoyi infection of the tongue.

pressure was 260, diastolic 90. The urine at first showed a specific gravity of 1.022, acid reaction, double plus albumin, no sugar nor acetone, numerous hyaline and granular casts, many white blood cells and a few red blood cells. Subsequent examinations showed only a trace of albumin and a few hyaline casts.

Study of electrocardiograms was summarized as follows: sinus rhythm; duration of cycle 0.76 corresponding to a rate of 79; P-R interval 0.16 seconds; QRS notched, but conduction time not prolonged; inversion of T2 and T3; left ventricular preponderance; frequent ventricular extrasystoles; P wave definitely notched throughout.

A teleroentgenogram revealed a transverse heart diameter of 19.6 cm. as compared with a transverse chest diameter of 25.3 cm. The heart outline was somewhat globular, resembling a pericarditis, although a myocardial change produces the same appearance.

Blood chemistry observations were nonprotein nitrogen 87 mg. per hundred cubic centimeters, creatine 1.8 mg. and sugar 87 mg.

Description of Organisms.—A direct examination of some of the material removed from the tongue, which had previously been cleansed with physiologic sodium chloride solution, showed the presence of many round and ovoid structures, from 3 to 5 microns in size, some with primary blastospores. A few mycelial threads were noted also. Sabouraud's medium was inoculated with this material which enabled us to classify the organisms under investigation. After twenty-four hours the colonies developed pinhead-sized white, creamy, elevated growths. These rapidly enlarged, with borders which were serpentine in form. Here and there were seen pinhead-sized growths which were darker and firmer in consistency.

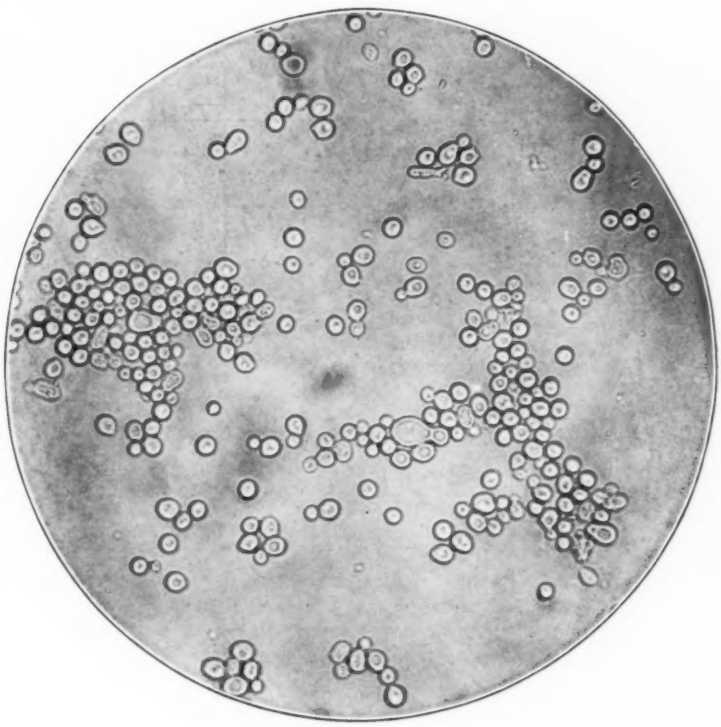

Fig. 2 (case 1).—Hanging-drop preparation from growth on Sabouraud's agar, showing mycelial rods and spores.

Two forms of organisms were seen under the microscope: (1) round and slightly elliptical, gram-positive, yeastlike cells from 3 to 5 microns in diameter, with distinct double-contoured border, a well marked large nucleus and many budding forms; (2) a mycelial form showing long, narrow, straight or septate rodlike mycelia with oval conidia. Chains of spores frequently appeared at each joint in the mycelium, and terminal and side branches were noted. This gave the appearance of a one-sided fruiting branch with the youngest chains of spores at the top and the oldest at the base. Detached globular cells (conidia) reproduced by budding. These two forms were isolated and pure cultures were made.

Description of Cultures and Fermentation Reactions.—The globular or yeast form (designated Z1 in the table) gave creamy white abundant growths on Sabouraud's medium. When young, mycelial elements were scant, but as growth conditions became more difficult through age and drying out of mediums, the filamentous portions were more in evidence. In dextrose broth, growth appeared as a delicate ring on the surface after three days' incubation at 37 C.; later the ring became more pronounced and a sediment formed. Short mycelial outgrowths were observed in older cultures in broth and milk. There was no change in reaction in litmus or milk, and gelatin was not liquefied. Fermentation reactions gave the following results: Dextrose, levulose and maltose were fermented with acid and gas production; galactose, saccharose, lactose, mannite, inulin and salicin showed only gas production.

Composite Table of Sugar Fermentation and Reaction in Litmus Milk and Gelatin *

	Z1 (Yeastlike)	Z2 (Mycelial)	K1 (Yeastlike)	K2 (Moldlike)
Litmus milk	0	As	0	As
Dextrose (glucose)	AG	AG	AG	0
Levulose	AG	AG	AG	0
Maltose	AG	G	AG	0
Galactose	G	Gs	G	0
Saccharose	Gs	0	AG	0
Lactose	G	Gs	Gs	0
Mannite	Gs	Gs	Gs	0
Dulcite	0	0	0	0
Dextrin	0	0	0	0
Adonite	Not tested	Not tested	0	Not tested
Inulin	Gs	Gs	Gs	0
Salicin	G	Gs	Gs	0
Trehalose	0	0	0	0
Xylose	0	0	Gs (?)	0
Glycerol	0	0	0	Not tested
Gelatin	0	0	0	0
Broth (dextrose)	Ring, later sediment	Delicate pellicle, later skinlike	Clear, with sediment	Thick pellicle
Agar slant (Sabouraud's medium)	White, raised, creamy, glistening	Dull, white, flat at first, later slightly raised	White, raised, creamy, glistening	Dull white, spreading (rhizoid)

* Table of sugars as arranged in Castellani and Chalmer's textbook: A indicates acid production; G, gas production; 0, no reaction but growth present; s, slight—for example, As indicates slight acidity.

The mycelial growth (designated Z2 in the table) produced on Sabouraud's medium pinhead-sized gray-white colonies, flat at first, and later more rugose and elevated, giving a radiating effect. In broth, a delicate pellicle and later a skinlike growth resulted. There was slight acidity in litmus milk and no effect in gelatin. The fermentation reactions were substantially the same as that of the yeastlike growth.

Sterile plaster-of-Paris blocks surrounded by sterile distilled water were inoculated with actively growing cultures of the two strains of fungi (about 24 hours old). These blocks were incubated at 37 C. for forty-eight hours and examined for the presence of ascospores at the end of twenty-four and forty-eight hours. No ascospores could be demonstrated.

Experimental Animal Inoculations (by Dr. Theodore K. Lawless).—For this part of the work sixteen full grown rabbits were used, ten for the yeastlike colonies and six for the mycelial forms. An emulsion was made in a 5 per cent

Fig. 3 (case 1).—Hanging-drop preparation of yeastlike growth.

Fig. 4.—Low power photomicrograph of kidney of rabbit on which inoculation had been performed, showing mycotic abscesses.

glucose medium, and injected intravenously. The average results were as follows: 1. After injection of the yeastlike culture the animals showed signs of toxemia in from three to five days, lifelessness, loss of weight and appetite and, finally, death from septicemia. On postmortem examination the spleen was found to be enlarged, the liver apparently normal and the lungs congested. The principal gross changes were found in the kidneys in the form of multiple miliary abscesses in the cortex. Pure cultures of the organisms were recovered from the heart blood, the liver and kidneys and were identical with the original growth. Animal passage increased the pathogenicity of the organism, the last group of rab-

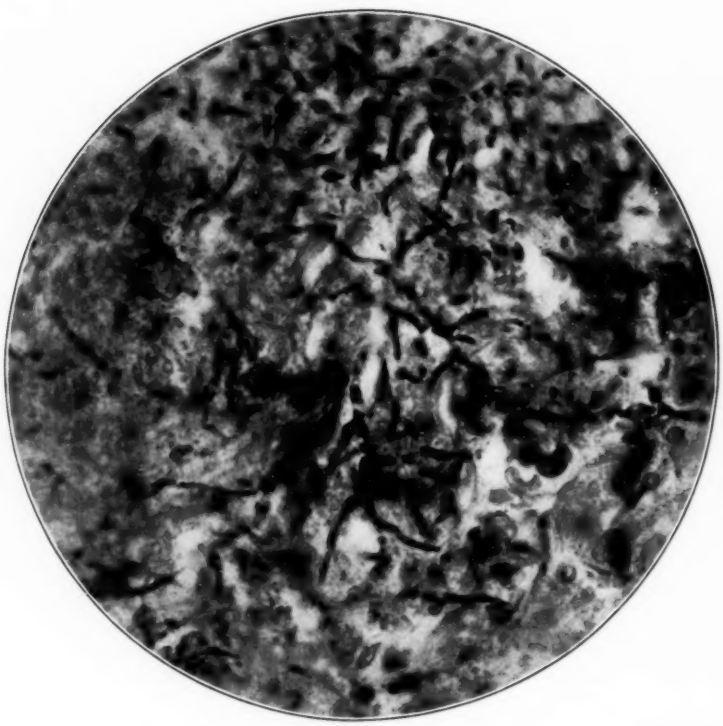

Fig. 5.—High power photomicrograph of monilia pinoyi as found in kidney of rabbit on which inoculation had been performed, showing branching mycelia and yeastlike bodies.

bits dying in twenty-four hours. Microscopically the renal lesions showed multiple mycotic abscesses containing the round and oval yeasts, with numerous elongated mycelial outgrowths of a granular or beaded appearance. 2. Injections of the mycelial suspension in the first two rabbits did not produce ill effects. The next four animals died on the average in from ten to fifteen days. General toxemia and emaciation were in evidence. The mycelia were recovered in pure culture from the heart, lungs, liver and kidneys. There was no gross pathologic condition in the kidneys, but on section many small cystlike structures were seen which contained a gelatinous material from which the organisms were grown. Similar cystlike structures were found in the liver. Attempts to reproduce the lesions

on the tongue by feeding cultures by mouth, and by scarifying the tongue and rubbing in cultures, were unsuccessful. Subcutaneous injections produced localized abscesses from which the yeasts and mycelia were recovered.

COMMENT

The impression gained from the study of the two strains of fungi isolated in this case is that there is a *Monilia* type of organism growing in the two forms, the yeastlike and the mycelial. The poly-

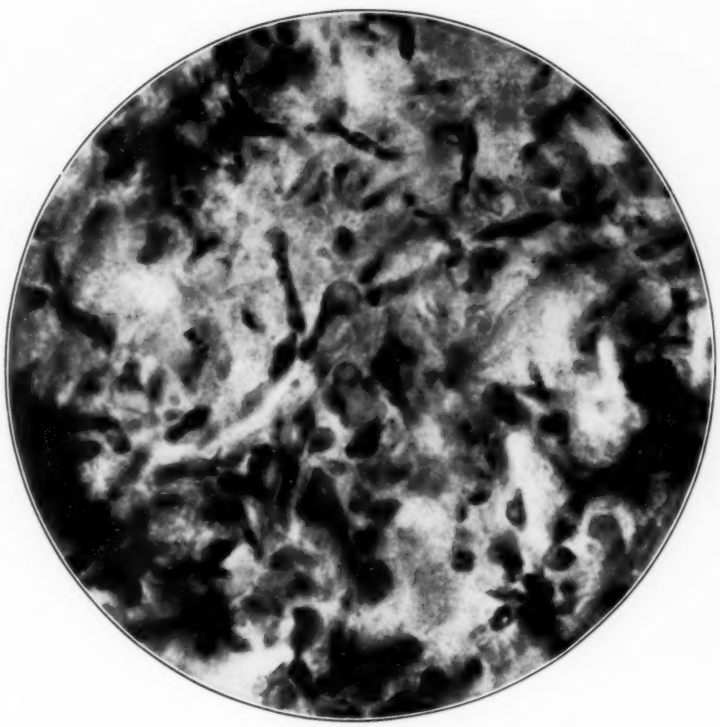

Fig. 6.—Oil immersion photomicrograph of monilia pinoyi as found in kidney of rabbit on which inoculation had been performed, showing yeastlike bodies with mycelial outgrowth.

morphism of this organism can best be explained by the results of the experimental inoculations which show that the two forms belong to one and the same fungus, the filamentous form developing most abundantly under adverse conditions of growth and representing the protective phase. In view of the morphology, the absence of ascospores and the sugar fermentation reactions, it appears to correspond most closely to the genus *Monilia pinoyi* (Castellani, 1910). This organism, although resembling *Monilia albicans* morphologically, differs in its reaction with milk, gelatin and sugar mediums.

Clinically the exanthem of the tongue in my experience is unique. A thorough search of the literature on tongue lesions (Butlin and Spencer, Mickulicz and Kümmel, Zinsser, Moral and Friboes, and others) has not shown an identical clinical picture. Fordyce and MacKee, in their recent comprehensive article on diseases of the oral mucosa, mention that they have seen one case of *Monilia* infection of the mouth. No doubt the condition is in many ways analogous to thrush. It can be readily differentiated from the various types of so-called geographic tongue which it most resembles. I believe, therefore, that it was an unusual mycosis of the tongue produced by *Monilia pinoyi* infection that I encountered. The association with polycythemia vera appears to be merely incidental. It is well-known that mycotic conditions of the mouth in adults (for example, thrush), although rare, may occur in the presence of severe organic disorders or cachexias in which the flora of the mouth is altered.

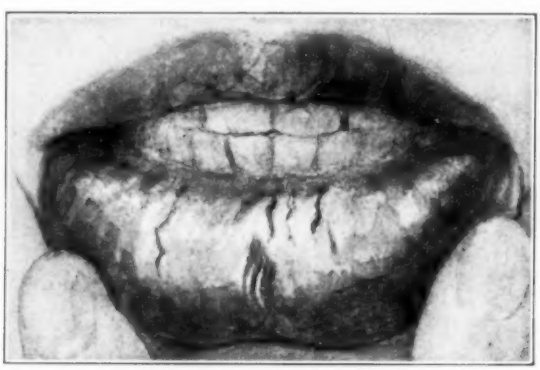

Fig. 7 (case 2).—Mycotic eruption of lips.

CASE 2.—*Mycosis of the lips and tongue, producing macrocheilia and macroglossia; demonstration of yeastlike fungus (cryptococcus) and a mold.*

History.—C. K., a man, aged 26, was referred by Dr. Lewis J. Pollock on account of an exanthem of the lips and tongue. The patient's mentality was of a low grade, and he was under treatment for convulsions. The condition of the mouth had been present for six months. He smoked cigarets to excess. He said that he did not have venereal infection.

Physicial Examination.—There was permanent alopecia of the scalp, evidently due to a healed favus. The heart and lungs were normal. The blood pressure was 110 systolic and 65 diastolic. The thyroid gland was moderately enlarged. The lower lip was markedly enlarged, and on palpation gave the impression of a doughy edema. The mucous membrane of the lower lip was covered with an irregular grayish-white, translucent pellicle, which could be scraped off readily. Several deep fissures were present beneath this. The upper lip and the inside of the mouth presented no abnormalities. The tongue as a whole was enlarged, the dorsum presenting numerous fissures and prominent papillae. On the lateral margins of the tongue were several narrow grayish translucent streaks, best described

by the German term "speckick." Under the tip of the tongue were several similar, not easily detachable, plaques. The throat was injected, but otherwise gave negative observations.

Laboratory Observations.—The Wassermann reaction was negative. The blood count was normal. A dark-field examination for spirochetes was also negative, as were smears stained for tubercle bacilli. Scrapings from the tongue and lip showed here and there a cluster of yeastlike organisms and delicate threadlike forms suggesting mycelia.

Description of Cultures.—Cultures on dextrose agar and agar plates at room temperature showed only a staphylococcus. In the incubator, cultures on maltose agar showed in seventy-two hours a mixed growth—staphylococci, fusiform bacilli, streptococci and round and oval budding yeasts. Eventually, I was successful in isolating the yeast which on Sabouraud's 4 per cent maltose peptone plants gave

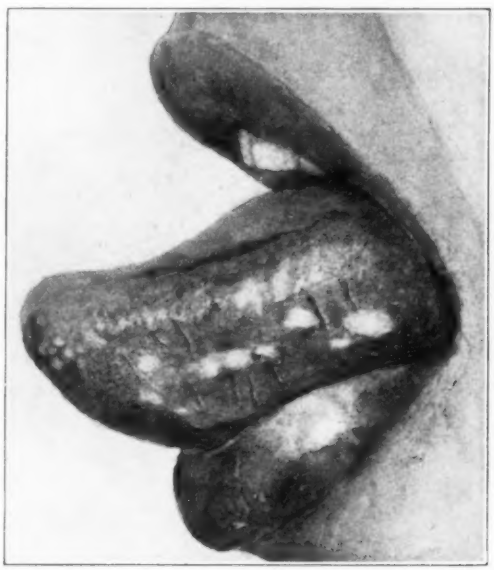

Fig. 8 (case 2).—Mycosis of tongue.

a smooth, whitish, glistening growth with a characteristic "yeast" odor. This was purified by plating methods before it was subjected to cultural reactions. Inoculation in litmus milk showed an abundant growth but no change in reaction. Small colonies, but no liquefaction appeared in gelatin. The fermentation reactions are given in the table (organisms designated K1). Ascospores could not be demonstrated and mycelial production was not satisfactorily shown, although the fungus was carefully observed in the laboratory for several months. The occasional elongated forms that were seen could hardly be called mycelia. Morphologically, the growth was a round or elliptical, deeply staining, gram-positive yeast which only reproduced by budding.

On a second occasion, cultures made from the scrapings from the tongue and lip showed the presence of a mold mingled with a streptococcus. The mold was isolated and showed mycelia with occasional septums and characteristic cylindrical conidia with truncate ends. The conidia appeared to arise from the side of the

mycelium. The mold grew in agar slants as a dull white schizoid, spreading growth, and produced a thick pellicle in broth, acid in litmus milk and gave negative fermentation reactions (designated K11 in table).

Animal Inoculations.—Rabbits were repeatedly inoculated intravenously with varying amounts of a culture of the live yeast and showed no symptoms of illness. At autopsy no pathologic changes were found. The kidneys showed no microscopic changes. Subcutaneous inoculation also was without result. Intravenous inoculation of the moldlike organisms produced no symptoms. At autopsy the kidneys were normal in gross and histologic specimens. The liver appeared to have small white nodular streaks similar to lesions of coccidiosis. The lungs and other viscera were normal.

Intracutaneous Test.—An intracutaneous test made with the yeast culture heated to 55 C. for one hour gave a positive inflammatory reaction in twenty-four hours. The controls gave negative results.

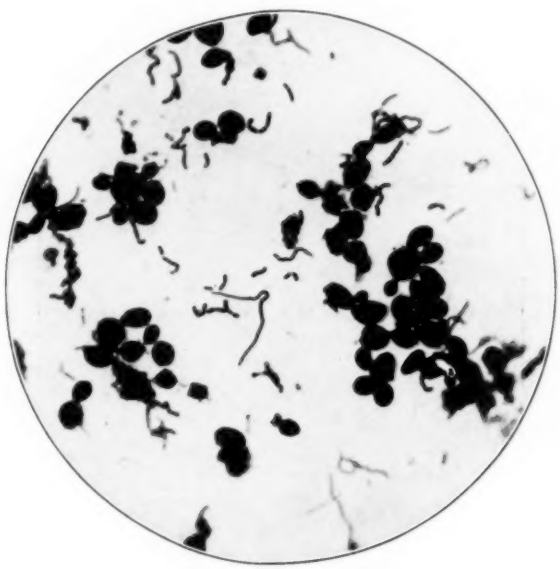

Fig 9 (case 2).—Stained smear from mixed growth on Sabouraud's agar, showing budding yeasts and other organisms.

COMMENT

My impression of the fungi grown in this case is that a nonpathogenic yeast and one of the common molds are being dealt with. There was no evidence of mycelial or ascus protection in cultures, and therefore, according to Castellani's classification, the yeast belongs to the cryptococcus group. The genus of the mold is undetermined. Whether the yeastlike form is responsible for the lesions in the patient's mouth is not definitely proved from the facts at hand, but the positive intracutaneous test and the presence of mycelia in scrapings is suggestive of a yeast or possible *Monilia* infection. The mold is regarded as a

saprophyte. It is, of course, entirely possible that the real fungus has not been isolated in this case. Clinically, the condition was interesting on account of the macrocheilia and macroglossia associated with the translucent, whitish, membranous eruption. It was felt that leukoplakia, syphilis, lupus erythematosus and lichen planus could be ruled out. The beneficial effect of iodine locally and the development of new patches from time to time favored the diagnosis of a mycotic infection. The condition is probably closely related to, if not identical with, thrush and invites comparison with Castellani's case of macroglossia caused by a yeastlike organism, which he at first ascribed to a cryptococcus and later decided was caused by monilia. This same observer has also reported a peculiar mycotic stomatitis with a thin translucent whitish membrane on the oral mucosa produced by the symbiosis of a yeastlike fungus (*Cryptococcus graciloides*) and a bacillus.

SUMMARY

Two unusual cases of mycotic infection of the mouth are described. The etiologic factor in one case has been established as *Monilia pinoyi*. The pathogenicity of this organism for rabbits and characteristic renal lesions are recorded. The second case is apparently associated with the presence of a nonpathogenic yeast of the cryptococcus variety and an unidentified mold. The literature on *Monilia* and monilia-like infections is reviewed with especial reference to conditions of the mucous membrane and the tongue. My observations confirm Castellani's view that thrushlike mycosis of the mouth may be caused by a variety of fungi.

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I am greatly indebted to Miss Janet M. Bourne of the Nelson Morris Institute of the Michael Reese Hospital for assistance in the fermentation reactions and in the animal inoculations in case 2.

ARSENIC LESIONS OF THE SKIN*

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Studies on metallic poisoning have been undertaken in syphilitic patients who were given routine treatment with arsenic preparations. The main object of the studies has been to determine whether or not certain organs respond to the administration of arsenicals, even though no clinical symptoms of metallic lesions appear in the patients examined. This was considered a starting point on which later studies could be based as to whether or not certain organs, particularly the skin, and their disturbances are responsible for the well-known symptoms of acute and chronic metallic poisoning.

THE INVOLUNTARY NERVOUS SYSTEM

Preliminary investigations along these lines have shown that a reaction of the involuntary nervous system occurs immediately after the injection of arsphenamine or neoarsphenamine in healthy as well as in syphilitic patients.[1] It is not yet known whether this reaction of the involuntary nervous system is essential for the therapeutic effect of the arsphenamines or only an effect which cannot be avoided when arsenicals are administered. Yet this reaction which has been described by us in a previous paper is always determinable when arsphenamine or neoarsphenamine is used intravenously in human beings as well as in animals. Such use of arsenicals is followed by a reaction of the vascular system which usually, however, is not noticeable to the patient. It is demonstrated by a sudden decrease of the leukocytes in the peripheric vessels for a short period, with a concomitant accumulation of these bodies in the region of the liver.[2] This indicates a previous

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* From the Department of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University. (Service of the late Dr. John A. Fordyce.)

1. Rosen, I.; Müller, E. F., and Myers, C. N.: Studies on the Complex Nitritoid Crisis After the Intravenous Administration of Arsenicals, Arch. Dermat. & Syph. **10**:316 (Sept.) 1924; The Relation of Silver Arsphenamin to the Involuntary Nervous System and to the So-Called Nitritoid Crisis, ibid. **10**:607-616 (Nov.) 1924.

2. Müller, E. F., and Myers, C. N.: Biochemical Studies on the Behavior of the Leucocytes After Intravenous Administration of Alkalinized Salvarsan, Proc. Soc. Exper. Biol. & Med. **22**:95, 1924.

disturbance of the vascular system in which the peripheric tonus suddenly turns to a sympathetic overbalance, the splanchnic region to a parasympathetic.[3] This is equalized after a short time. Patients showing symptoms of nitritoid crisis have a much stronger reaction measurable in a deep leukocyte fall, lasting for the period of the clinical symptoms.

By the method described it has been possible to determine the participation of the involuntary nervous system not only in patients with visible symptoms of shock, but also in all patients and healthy persons injected with a therapeutic amount of arsenic such as is contained in a dose of arsphenamine. Our investigations have not enabled us to determine whether or not the involuntary nervous system shows a difference from the normal stage during a later period, but it is probable that it does.

EXCRETION OF ARSENIC

From the chemical determinations of the distribution of arsenic in the body it is known that arsenic disappears rapidly from the circulation after the injection of the different arsphenamines.[4] As this amount of arsenic lost from the blood stream is not excreted it is assumed that it is deposited in all the different organs.

Furthermore, it is known from the same chemical studies that arsenic is excreted from this time on for a period of some weeks. The excretion takes place by way of the kidneys, the liver and the skin. After the first sudden decrease, the amount of arsenic in the blood gradually increases from the seventy-second to the ninety-sixth hour after the injection. It then maintains a nearly constant level of 1 mg. of arsenic in 100 Gm. of dried specimen. Since the level remains constant although arsenic is being eliminated continuously, it seems probable that the arsenic which is being released from its storage places in the body into the circulation will be passed from the blood to all parts of the body; one part of the arsenic will go into the excretory organs—the kidneys and the liver—and other parts carried by the circulation will again be accumulated in those tissues and organs in which it was previously stored.

The work of Fordyce, Rosen and Myers in analyzing thousands of specimens from human beings and rats gives a good picture of this complicated excretory process. It indicates clearly that a well regulated

3. Müller, E. F.; Ueber eine gemeinsame vegetative Steuerung von Haut und Lebergebiet, München. med. Wchnschr. **73**:9 (Jan.) 1926.

4. Fordyce, J. A.; Rosen, I., and Myers, C. N.: Quantitative Studies of Syphilis from a Clinical and Biological Point of View: II-XVII, Am. J. Syph. **7**:209, 225, 444, 478, 513 and 528, 1923; **8**: 34, 65, 193, 264, 297, 377 and 619, 1924; **9**:18, 1925; Am. J. M. Sc. **164**:492, 1922; Arch. Int. Med. **31**:739 (May) 1923. Fordyce, J. A., and Myers, C. N.: Am. J. Syph. **9**:490, 1925.

excretory function consists of a balance between the organs which gradually pass deposits from their tissues into the circulation and receive arsenic by blood distribution and the real excretory organs, which eliminate the arsenic by natural channels.

The nearly constant level maintained in the blood for weeks, in spite of the continuous flow from the arsenic deposits, favors the assumption that all these single processes are commonly controlled.

ARSENIC IN THE CIRCULATION

The foregoing facts are gained from determinations in patients without acute or latent symptoms of lesions produced by arsenic. If one compares the chemical determinations of these normal patients with those of others who show clinical symptoms of arsenic poisoning or a poisoning influence of arsenic on the skin, for instance, a remarkable difference is found. From the onset of the clinical observations until the disappearance of the skin symptoms, no considerable amounts of arsenic can be found either in the circulation or in the excreted urine or feces. The reason for this can be given only briefly in this article.

Studies on the relation between the skin and the involuntary nervous system have led to the following observations: Under normal conditions, the vessels of the entire body are kept in a certain tonus which depends on a balance between vasodilating and vasocontracting impulses carried by the vasomotor system to every vessel. If the vasomotor system reacts to disturbances of various kinds, this reaction always produces manifestations at the site of the vessels. The reactions are opposite in character in the peripheral and the splanchnic areas. If one of the two groups of organs reacts with dilatation, the other simultaneously shows contraction, and vice versa. Usually all vasomotor reactions occur in alternating contractions and dilatations. From the same studies it also developed that during such alternating movements the two areas were always characterized by opposite reactions. The manifestations of the opposite reactions are particularly obvious in the skin and in the liver. This opposite tonus is apparent whenever a vasomotor reaction occurs. In the same way it was demonstrated that real disturbances of the involuntary nervous system, when they occur, are manifest immediately in loss of control of vessel activity as well as of the activities of certain physiologic functions of the two groups of organs, splanchnic and peripheral.

In disturbances of the vasomotor nerves by a prolonged circulation of arsenicals in the blood over a protracted period of time, two principle excretory organs, the liver and skin, lose their power not only of excreting arsenic from the body but also of transferring arsenic and probably other products of metabolism from their tissues to the circulation. From the continued studies carried out by Fordyce, Rosen and Myers

on the distribution of arsenic, after using arsenicals, it is assumed that a steady circulation of arsenic from one organ to the other exists. Every organ receiving arsenic again and again from the circulation passes this metal back to the blood stream because, like all proteins, it cannot be assimilated by the tissue cells. While the first action, the passing of arsenic from the circulatory system to the organs and tissues, must be considered merely as a passive process, the repassing of arsenic from the tissues to the blood stream is possible only by means of an active function of the tissue cells, i. e., of the organs involved. It is a dynamic action like that of excreting metabolism products from the liver by way of bile formation that has to be distinguished sharply from the secretion of metabolism products into the body fluids, even if it is known that both actions of the organs are so closely related to each other that by losing certain physiologic activities both actions will be diminished at the same time. In the meantime, however, the other organs continue to pass arsenic from the deposits in their tissues into the blood. The blood, in the natural course of its circulation, carries the arsenic to the skin and liver where it accumulates because these organs have lost their ability to excrete and to pass it to the circulation. Thus, the arsenic content of the circulation is kept low so that little or no excretion is accomplished by way of the kidneys. An accumulation of arsenic in the organs affected leads to an increase of the metal which cannot be tolerated by the living cells.

Clinical, pathologic and chemical observations point to two distinct stages of metallic intoxication of the skin. The first phase consists of the diminution or loss of the function of the skin and of the liver. At the same time, these organs lose their controlled resistance against a too extensive diffusion of arsenic from the circulation into their tissues. The second phase is the local influence of the too highly concentrated metal on the cells.

These two stages of metallic intoxication must be distinguished sharply. The first is a systemic functional disturbance, while the second is the definite accumulation of arsenic resulting from the first stage and a purely local disturbance of the cells caused by the excessive concentration of arsenic present in the tissues.

SKIN LESIONS

The clinical observation of reactions occasionally occurring after the injection of arsenicals shows that they consist of angioneurotic phenomena in almost the entire body, including the skin, liver, lungs and heart. They disappear rapidly although there is no doubt, either clinically or experimentally, of their dependence on a primary reaction of the vasomotor system. It may be repeated that in all patients receiv-

ing intravenous arsphenamine treatment similar reactions of the vasomotor system can be demonstrated, the intensity of which is so small that it can be found only by blood examinations.

If lesions due to arsenic intoxication appear generally as an erythema, no matter whether they occur simultaneously all over the body surface or whether they concern only certain areas, the first symptoms are typical vasomotor disturbances. They resemble the onset of dermatitis venenata, and the eruptions following the intake of certain foods or contact with pollen in highly sensitive patients. The main symptoms indicating such a systemic vasomotor disturbance are the simultaneous onset, the prevalence of vasculary symptoms, almost alike in all involved parts of the skin even if the eruption concerns the entire surface, fever, disturbances of the digestive tract such as nausea and vomiting and a general feeling of malaise. Although vasomotor disturbances observed with other harmless drugs or with reactions after touching pollen may disappear rapidly, they are followed in arsenic dermatitis, by a prolonged and sometimes fatal stage. The severe degenerative local lesions are caused by the gradual increase of arsenic in the area. The clinical picture agrees with the chemical arsenic determinations. Accumulation of arsenic in the skin has been proved by the analyses of the scales representing such dead parts of the involved skin, which show that the amount of arsenic in the skin increases with the increasing severity of the skin lesions.

CHRONIC IRRITATION

The first symptoms of nitritoid crises and the clinical observations as well as chemical determinations of the arsenic show that a functional disturbance of the skin, and probably also of the liver, precedes the accumulation of arsenic in the involved organs. This indicates that a disturbance of the vasomotor system controlling these organs plays an important part in arsenic intoxication. The first reaction of the vasomotor system can be determined as mentioned above. It must be assumed that there remains a chronic irritation due to the continuous presence of arsenic in the circulation even if no methods of determining this are known.

The onset of a detectable disturbance of the vasomotor system indicates only that a point of hyperirritation has been reached. From clinical experience it is assumed that the amount of arsenic is not the only factor responsible for this hyperirritation; otherwise, every patient must suffer from metallic intoxication after the same quantity of the metal has been administered. Probably, a varying individual resistance toward arsenicals exists, which, in the main, involves the involuntary nervous system controlling the vegetative functions of all organs. It is known that this hyperirritation is not due to an overdosage of arsenic

because often no arsenic has been administered for several days or even weeks previously. There must, therefore, be a continuous irritation, which at the time when clinical symptoms occur reaches a "breaking point" and produces the well-known manifestations of the vascular system, coupled with the loss of controlling power.

DISTURBANCE OF METABOLISM

If the symptoms of arsenic dermatitis improve or disappear, the arsenic content of the circulation increases and the excretion of the arsenic by way of the kidneys and the liver, demonstrable in the urine and the feces, begins again. This indicates that the skin has regained its power to pass arsenic into the circulatory system and has reestablished its resistance against the diffusion of too high quantities of arsenic into the tissues. Thus the increased concentration in the blood again makes elimination by way of the kidneys possible. This clinical and chemical observation indicates a stage in which the control of the skin metabolism is regained, excretion of the skin deposits becomes possible and the clinical skin involvement improves. If this stage is reached early, no dangerous lesions remain in the skin, because the period in which a highly concentrated metal has been present in the skin has been too short to destroy vital parts of the skin tissues. If the stage of metabolism disturbance continues over a considerable period, the lesions, as is well known, are dangerous and even fatal, if too large areas are involved.

SODIUM THIOSULPHATE

Dennie and McBride [5] were among the first to succeed in relieving arsenic intoxication of the skin in patients treated with arsphenamine by the intravenous administration of sodium thiosulphate. The theory of this clinic and therapeutic observation has been that sulphur is able to change insoluble arsenic compounds developed in the skin to soluble ones and thus make their excretion possible. The explanation does not satisfactorily account for the action of the drug, because more recently our studies on biologic functions of the skin, as partly described in this paper, indicate that the action of sodium thiosulphate is more far-reaching than the suggestion offered. In this brief report no detailed explanation can be given.

The observations after early administration of sodium thiosulphate are as follows: The clinical manifestations in the skin disappear gradually and frequently in a short time. Other systemic disturbances

5. McBride, W. L., and Dennie, C. C.: Treatment of Arsphenamin Dermatitis and Certain Other Metallic Poisonings, Arch. Dermat. & Syph. **7**:63 (Jan.) 1923; Treatment of Arsphenamin Dermatitis, Mercurial Poisoning and Lead Intoxication, J. A. M. A. **83**:2082 (Dec. 27) 1924.

disappear simultaneously. During this period arsenic reappears in the circulation and in the excretion, indicating that deposits of arsenic are being passed into the blood. This phenomenon must be explained as follows: The irritation of the vasomotor system causing the functional disturbance of the skin, particularly its power of secretion and diminishing the resistance of the skin tissues to the deposition of arsenic, is almost immediately relieved by the administration of the sulphur preparation. The reason is unknown, but the fact exists. The same clinical and chemical observations follow the early administration of sodium thiosulphate as those which accompany a natural cure of similar lesions.

If sodium thiosulphate in the same amounts is given at a later date, no further improvement can be obtained and no more arsenic reappears in the circulation. If the action of sodium thiosulphate is only to change the insoluble arsenic compounds into soluble ones, then there is no reason why smaller amounts of arsenic cannot be made soluble at a later date. On the other hand, if the deleterious effect of the highly concentrated arsenic has actually destroyed the skin tissues to a certain extent, then even the regained control of the involuntary nervous system can no longer act, because the substance which has to perform the excretory processes is destroyed.

SUMMARY

1. Skin lesions, as known in certain persons after treatment with arsenicals, depend on a primary disturbance of the involuntary nervous system.

2. The involuntary nervous system shows slight reactions immediately after injections of arsphenamine.

3. The continuous presence of arsenic in the circulation produces a continuous slight irritation of the involuntary nervous system.

4. This irritation does not lead to dangerous symptoms as long as a certain limit is not passed.

5. In certain persons the same continuous irritation results in hyperirritation of the involuntary nervous system, and simultaneously with the onset of this hyperirritation, the organs depending mainly on the control of the involuntary nervous system show disturbances of their physiologic functions. This is manifested clinically by angioneurotic symptoms and chemically by a diminished resistance of the organs against deposition of arsenic in abnormal concentrations in their tissues and in a disturbance of their function to excrete and secrete metabolism products.

6. With this disturbance of the skin metabolism following the primary disturbance of the involuntary nervous system, an accumulation of arsenic in the skin occurs, producing local lesions in the tissue cells.

7. If the controlling power of the involuntary nervous system is reestablished, naturally or by therapeutic means (sodium thiosulphate), the normal physiologic functions of the skin are regained, whereupon arsenic is passed from the skin to the circulatory system and excreted by way of the natural channels.

8. If this reestablishment of the controlling power is not gained before vital parts of the skin tissues have been destroyed by the locally toxic, highly concentrated and gradually increasing arsenic deposits, restored autonomic nervous control will no longer result in a cure.

9. Dermatitis or erythema following the use of arsphenamine is a disease of the involuntary nervous system appearing in persons whose involuntary nervous system does not tolerate a continuous irritation arising from the administration of certain amounts of arsenic tolerated by others. The reason for this phenomenon may be that there is a constitutional difference or a previous damage of the involuntary nervous system by syphilitic infection. The latter is curable if the irritation is relieved early enough; it is not curable if vital parts of the skin are already destroyed. Lesions of the skin after the administration of arsphenamine do not depend on a special toxicity of the injected arsenic preparation but on the individual susceptibility of the involuntary nervous system to like concentrations of arsenic in blood and tissues.

PURPURA HEMORRHAGICA FOLLOWING SULPHARSPHENAMINE

REPORT OF A CASE

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During the last few years, from time to time, cases have appeared in medical literature, presenting a blood picture suggestive of an aplastic pernicious anemia with cutaneous hemorrhages and no apparent visceral changes following treatment with neoarsphenamine and sulpharsphenamine, particularly, the former. Every one who has treated many patients with syphilis has occasionally been unfortunate enough to have had a toxic effect of medication with cutaneous manifestations. I am reporting the first hemorrhagic case which I have observed, after approximately four thousand injections of the arsphenamines. Its exceptional severity and unusual character, coupled with several points of particular interest, seem sufficient to warrant a brief report and discussion.

REPORT OF CASE

History.—A. B., a man, aged 54, married, was sent to me in the summer of 1925 with definite physical signs of beginning tabes dorsalis. The Wassermann reaction was four plus to both alcoholic and cholesterinized antigens in the blood and spinal fluid. He had had a chancre some twenty years previously which was treated by cauterization and a short course of mercury tablets by mouth. He had had no further physical evidence of the infection.

Treatment.—I prescribed potassium iodide up to one dram (4 cc.) three times a day, with inunctions of mercurial ointment. During the months of September and October he received eight weekly injections of arsphenamine, 0.4 Gm. each. The blood Wassermann reaction on December 3, was two plus with the cholesterinized antigen, and negative with the alcoholic antigen. His health had improved greatly. At this time he left the city and took mercury by mouth for about three months.

On his return, I gave him intramuscular injections of bismuth and sulpharsphenamine intravenously, as follows: June 4, 0.3 Gm. sulpharsphenamine; June 11, 0.4 Gm.; June 18, 0.4 Gm.; June 25, 0.4 Gm.; July 2, 0.4 Gm.; July 13, 0.4 Gm.; July 28, 0.4 Gm.

On August 25 he complained of pains of a boring nature in his ankles, particularly the left one. On examination, I noticed many confluent cutaneous hemorrhages. These varied in size from that of the most minute telangiectatic puncta to that of a pea. For the most part they were bright in color, although some were bluish or dusky red. They were not elevated, and were most numerous about the lower leg and ankles, disappearing at about the knees. These had been present about a week, and even then the patient probably would

not have called my attention to them had it not been for the associated pains. It was necessary for him to take a two weeks business trip at this time. I gave him salicylates internally, which were effective in controlling the pain.

On his return, he complained of bloody stools and bleeding from the gums, which had been growing worse for a week. I immediately put him to bed in the hospital and gave him an astringent mouthwash and suppository, with calcium lactate internally — 1 dram (4 Gm.) divided into four doses, one every four hours.

In order that a clearer conception may be had of the clinical progress of the case, I have outlined its course chronologically.

September 3. *Physical Examination.*—The temperature was 102, the pulse rate 88, respirations 20.

Head: The pupils were contracted and did not react to light. There were a few small hemorrhages surrounding the disk of the right retina. The conjunctivae were pale. The skin of the face was clear, except for a purpuric spot the size of a quarter dollar on the right temple. The submaxillary gland on the left side was moderately enlarged and tender, probably because of the absorption of purulent material from the mouth. Bleeding from the gums and mucous membranes of the cheeks was profuse. There were several purpuric areas on the cheeks, and one, the size of a dime, on the dorsum of the tongue. This was slightly raised and suggestive in appearance of noma. The gums were soft, somewhat receded and hemorrhagic. Large clots formed along the mucobuccal fold which came away without much difficulty, leaving an oozing surface beneath. The teeth were in good condition: a roentgen-ray examination had been made at the onset of the reaction.

Chest: The skin and internal organs of the chest showed no evidence of involvement. There was a palpable lymphatic gland in the left axilla about the size of a hazelnut.

Abdomen: Nothing pathologic was evident, except bleeding from the anus. Proctoscopic examination revealed two hemorrhagic areas about the size of a thumb-nail on the rectal mucous membrane. There was also a slight weakness of the sphincter.

Extremities: The hemorrhagic areas in the skin of the legs were no more extensive than when I had examined him nearly two weeks previously, but on the contrary seemed to be fading. The knee-jerks were exaggerated; Babinski's reflex was present, with the suggestion of ankle clonus.

Subjective symptoms: The patient complained of severe headaches, throbbing in the ears and intermittent pains in the ankles. His appetite was excellent and his mental poise perfect.

Medication: Sodium cacodylate, 1½ grains (0.9 Gm.) daily, was administered intramuscularly, and horse serum, 5 cc. subcutaneously.

Laboratory Examination.—Examination of the blood revealed: white blood cells, 1,900 per cubic millimeter; red blood cells, 2,810,000 per cubic millimeter; hemoglobin content, 40 per cent; color index, 0.7; bleeding time, 6 minutes, thirty seconds; coagulation time, 4 minutes, forty seconds; icterus index, 5; blood platelets, 175,000. The differential count revealed: red cells — moderate central pallor, occasional poikilocytes, moderate anisocytosis, few macrocytes, moderate numbers of microcytes and no blasts; white cells — 16 per cent polymorphonuclears (304 per cubic millimeter), 80 per cent lymphocytes (1,520 per cubic millimeter) and 4 per cent large mononuclears (76 per cubic millimeter).

Urinalysis: The urine was normal except for a faint trace of albumin.

September 4 to 6. The patient's condition remained about the same, although the bleeding from the gums gradually subsided. The hemoglobin content dropped off to 30 per cent. On September 6 a direct blood transfusion of 850 cc. was given, following which the temperature fell to normal and the patient showed some improvement.

September 8. Examination of the blood revealed: white cells, 1,900 per cubic millimeter; red cells, 1,850,000 per cubic millimeter; hemoglobin content, 37 per cent; color index, 1.0, and blood platelets, 110,000. The differential count revealed: red cells — marked central pallor, occasional poikilocytes, moderate polychromatophilia, marked anisocytosis, few macrocytes, few microcytes and no blasts; white cells — no polymorphonuclears, 66 per cent small lymphocytes (1,254 per cubic millimeter), 28 per cent large lymphocytes (532 per cubic millimeter), 4 per cent large mononuclears (76 per cubic millimeter) and 2 per cent transitional cells (38 per cubic millimeter).

September 10. The temperature again rose and fluctuated between 101 and 104 F. Another blood transfusion of 850 cc. was given, but the patient gradually failed. There was no further bleeding.

September 11. Examination of the blood revealed: white cells, 500 per cubic millimeter; red cells, 2,210,000 per cubic millimeter; hemoglobin content, 47 per cent; color index, 0.7. The differential count revealed: red cells — moderate central pallor, occasional poikilocytes, marked anisocytosis, no polychromatophilia, many macrocytes, few microcytes and no blasts; white cells — 7 small lymphocytes and 2 large lymphocytes (only 9 cells found on the entire slide).

The patient had an uncomfortable day, the temperature mounting to over 104 F., and the pulse increasing in rate and failing in volume. He suffered paralysis of the bowel, urinary bladder and anal sphincter, resulting in prolapse of the rectum. Death intervened early September 12. Permission for a necropsy could not be obtained.

COMMENT

In the following comment I have especially neglected mention of the biochemical effects of the arsphenamines on the human organism, since my interest is chiefly in the clinical aspects of the case. In choosing a title, I decided on purpura hemorrhagica for two reasons, first, since it is considered, from a dermatologic point of view as a distinct clinical entity. Secondly, cutaneous hemorrhage was the prevailing symptom. However, to say that the patient succumbed to purpura hemorrhagica would be a gross misrepresentation of facts, the cutaneous bleeding being merely a manifestation of some organic derangement of the blood-forming tissues, effecting the permeability of the capillary endothelium.

The first hemorrhages made their appearance approximately ten weeks after the first injection of sulpharsphenamine and two weeks after the last injection. The dosage had been moderate, there being no necessity for more intensive treatment, and the administrations had been accompanied by no immediate reactions.

The blood pictures indicate an acute interference with the production of the granular elements, namely the polymorphonuclear leukocytes, basophils, eosinophils and blood platelets. In reducing the percentages

to actual numbers per cubic millimeter it will be observed that although there is a relative lymphocytosis, actually the numbers are nearly normal. Furthermore, there was no clinical evidence of disease of the lymphatic system.

Another apparent point is that there is no evident destruction of the erythrocytes in the blood stream, nor any increased destruction in the liver, the icterus index being well within normal limits.

Medical literature is not profuse in hemorrhagic cases following treatment with sulpharsphenamine. Weil and Isch-Wall [1] reported ten cases of purpura similar in nature to my own following treatment with the arsphenamines, although none of them appears to have been as severe. The bleeding time or coagulation time in their cases were not given. However, they were probably unaltered, because if the arsenobenzols produced a purpuric syndrome, as a result of their anticoagulating action, there would be a similar sequel in all cases in which injections were made.

Gaviot [2] viewed the purpuric cases rather lightly apparently attributing them to anaphylaxis, developing within a few hours after the injection.

Chantellier [3] reported a case with death following eleven injections of neoarsphenamine which was evidently similar to my own. However, the necropsy revealed nothing.

Callomon,[4] in 1922, reported a case following two small doses of neoarsphenamine which also terminated fatally. Necropsy showed hemorrhagic areas throughout the body with the exception of the intestines. In this case, however, there was an increase in the blood platelets.

Anwyl-Davies [5] reported an interesting case in a woman, following treatment with neoarsphenamine. The condition appeared twelve hours after the last injection, the previous injections having extended over a period of three months. The lesions cleared up in a week's time, and the patient made an uneventful recovery. He is of the opinion that "the condition may be similar in nature to those cases of epileptiform convulsions following injections, in which postmortem examination showed punctate hemorrhages in the brain, and attributable to damage of the capillary epithelium by the remedy." In view of the definite blood changes present in these cases, I cannot conform to his opinion, but am inclined to believe that the injury to the capillary endothelium is secondary to changes wrought in the bone marrow.

1. Weil, E., and Isch-Wall, P.: Presse mèd. **31**:657, 1923.
2. Gaviot, C.: Vie méd. **4**:1113, 1923.
3. Chantellier, L.: Bull. Soc. franç. de dermat. et syph. **30**:51, 1923.
4. Callomon, F.: Dermat. Wchnschr. **75**:1197 (Dec.) 1922.
5. Anwyl-Davies, T.: Brit. J. Dermat. **33**:264 (July) 1921.

In this country, C. Morton Smith[6] of Boston reported a case following treatment with neoarsphenamine in which the patient recovered. Unfortunately he was unable to study the case thoroughly as he did not see the patient until complete recuperation of the hematopoietic system had taken place.

The literature is profuse in reports of aplastic anemias following benzene poisoning, which presents a clinical and blood picture similar to the case under discussion. In view of the benzene basis of the arsphenamines, I regard the hemorrhagic reaction of the organism to benzene and sulpharsphenamine as the same in nature; namely, an intoxication of the blood-forming organs, in all probability, the bone marrow, with secondary injury to the peripheral capillary circulation, resulting in a faulty production of the granular leukocytes, and subsequent loss of the nongranular elements of the blood; producing an aplastic and pernicious anemia, recovery from which is dependent solely on the extent of injury done to the bone marrow. This is true notwithstanding the fact that anemias following benzene poisoning are hemolytic and accompanied by a high icterus index.

The advent of this hematopoietic crisis cannot be anticipated, nor can it be avoided by any test of liver function, of blood coagulability or for previous evidence of hemophilia or hemorrhagic diathesis. The only possibility of averting death rests on early recognition. Transfusion appears to be the method of treatment on which most reliance can be placed.

80 West Fortieth Street.

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6. Smith, C. M.: Severe Bleeding and Purpura Following Administration of Neoarsphenamin, Arch. Dermat. & Syph. **11**:237 (Feb.) 1925.

News and Comment

ARKANSAS

Special Courses at Hot Springs.—The Surgeon General, U. S. Public Health Service, announces that special courses in the control and treatment of venereal disease will be given at the venereal disease clinic of the public health service at Hot Springs, for physicians, clinicians and health officers. Fees will not be charged for the course but the individual physician will necessarily pay his own expenses for living and travel. The classes will be held in the new building in which the clinic is operated, where, last year, 3,570 indigent persons were examined and 3,064 cases of syphilis and gonorrhea diagnosed. There are exceptional facilities for the study of venereal disease, especially for diagnosis, treatment and clinic management. The courses will consist of lectures by specialists attached to the clinic and demonstrations, as well as practical experience in diagnosis and treatment. New courses of not more than ten will form on the first day of each month and will continue for a minimum of thirty days, and those who complete the work satisfactorily will be presented with an engraved certificate by the public health service. The courses are part of the cooperative work with the state health departments in the control of venereal diseases. Applications of physicians to take the course should be endorsed by the state health department in which the applicant resides before being submitted to the Surgeon General, U. S. Public Health Service, Washington, D. C.

CALIFORNIA

Proposal to Prevent Beauty Parlor Deaths.—Reiterating that at least a dozen deaths have occurred in California from the promiscuous use of preperations and processes employed by "beauty specialists," the secretary of the state board of medical examiners, Dr. Charles B. Pinkham, stated, November 3, that a bill would be introduced into the next legislature to prohibit "beauty specialists," except those who may be licensed physicians, from using dangerous drugs in their work.

MASSACHUSETTS

Resignation and Appointment at Harvard.—Dr. C. Morton Smith has recently resigned as clinical professor of syphilology at the Harvard Medical School, and his place is to be filled by Dr. Henry D. Lloyd, for some time instructor in syphilology. Dr. Lloyd's title is "assistant professor of syphilology."

MARYLAND

Election.—Dr. Jere W. Lord, Baltimore, has been elected president of the Baltimore-Washington Dermatological Society for the ensuing year and Dr. Frank J. Eichenlaub, 900 Seventeenth Street N.W., Washington, D. C., secretary.

GENERAL

Appointment.—Samuel W. Becker, M.D., of Zurich, has been appointed fellow of the National Research Council.

MADRID

Appointment.—Dr. José Sánchez Covisa, the dermatologist of the San Juan de Dios Hospital, has also won in a competitive examination the vacant chair of dermatology in the Madrid Medical School. Sánchez Covisa has already made a name for himself in skin diseases in Spain.

DEATHS IN OTHER COUNTRIES

Death of Dr. Ehrmann.—Salomon Ehrmann, professor of dermatology and syphilology, University of Vienna, aged 72, October 24, of heart disease.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up-to-date.

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MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY
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George D. Culver, Secretary, 323 Geary St., San Francisco.

Abstracts from Current Literature

CHANCROIDAL BUBOES: EFFICIENT TREATMENT BY INJECTIONS OF MENCIÈRE'S SOLUTION. H. G. MISKJIAN, J. A. M. A. **87**:1436 (Oct. 30) 1926.

The solution consists of iodoform, 10 Gm.; guaiacol, 10 Gm.: eucalyptol, 10 Gm.; alcohol, 95 per cent, 10 Gm.; balsam of Peru, 30 Gm.; and ether 100 Gm. The injection is made one or more days after incision of the bubo, and repeated in seventy-two hours if necessary.

The author has treated twenty-five patients by this method, with prompt success in twenty-three. In about two thirds of the cases, only one injection was necessary.

SPECIFIC NECROSIS IN THE INFECTIOUS GRANULOMAS: DEMONSTRATION IN THE TESTIS IN EXPERIMENTAL TUBERCULOSIS, BACILLUS ABORTUS INFECTION AND BLASTOMYCOSIS. E. R. LONG, J. A. M. A. **87**:1441 (Oct. 30) 1926.

Long's investigation showed that hypersensitiveness of tissue cells to the infecting agent of a chronic infection renders those cells liable to necrosis when the infecting agents or products derived from it come into contact with them. In guinea-pigs with tuberculosis, infection with *Bacillus abortus* and blastomycosis, the injection of tubercle bacilli, abortus bacilli and blastomyces, respectively, or culture medium filtrate from these micro-organisms into the testis, leads to necrosis. Hypersensitiveness is more easily demonstrated experimentally in the testis than in the skin—and in blastomycotic infection in guinea-pigs the skin is insensitive, while the testis is in an allergic state.

HODGKIN'S DISEASE WITH SPECIAL REFERENCE TO ITS TREATMENT BY IRRADIATION. C. F. BURNAM, J. A. M. A. **87**:1445 (Oct. 30) 1926.

Burnam's report is based on 173 patients treated at the Howard A. Kelly Hospital between 1913 and 1925.

In an analysis of the symptomatology of this group of cases, pruritus was noted as an initial symptom in twelve cases, and occurred at one time or another in fifty-five cases. Skin lesions of a toxic character were present in twenty-one cases. Most of the skin lesions improved with the improvement in the general condition, but two cases of erythroderma were uninfluenced by any measure. In only two instances were there true pseudoleukemic infiltrations in the skin.

Burnam's experience with radiation leads him to prefer radium to the roentgen ray. In his series, twenty-eight patients were clinically cured, and definite and protracted palliation was secured in many others.

THE VALUE OF THE STUDY OF HISTOPATHOLOGY IN CUTANEOUS MEDICINE. W. J. HIGHMAN, J. A. M. A. **87**:1459 (Oct. 30) 1926.

Highman points out the value of cutaneous microscopic changes to the dermatologist and criticizes the apparent lack of study of these changes evidenced in American papers.

VARIATIONS IN CUTANEOUS TOLERATION FOR ROENTGEN RAYS. G. M. MACKEE and J. J. ELLER, J. A. M. A. **87:**1533 (Nov. 6) 1926.

The authors found that about 5 per cent of a large series of persons developed an erythema after one-fourth skin units of unfiltered roentgen rays, 15 per cent after one-half, and 25 per cent after three-quarters units. They suggest that the patient's skin be tested for tolerance to roentgen rays before a course of treatment is instituted.

There is, as is well-known, considerable variation of susceptibility to roentgen rays and also some evidence to support the belief that mild grades of idiosyncrasy exist.

STIMULATION AND IMMUNITY IN RADIOTHERAPY. A. W. DESJARDINS, J. A. M. A. **87:**1537 (Nov. 6) 1926.

In a general review of the evidence relating to these questions, Desjardins concludes that the roentgen rays neither have stimulating action nor do they enhance immunologic reactions in tissues.

INTERSTITIAL KERATITIS IN CONGENITAL SYPHILIS: CLINICAL NOTES ON INCIDENCE AND TREATMENT. W. H. GUY, J. A. M. A. **87:**1551 (Nov. 6) 1926.

Guy found an incidence of 1 per cent of syphilitic keratitis in 15,000 opthalmic cases. Of his 160 cases of syphilitic keratitis, 150 occurred in congenitally syphilitic patients.

The patients were given antisyphilitic treatment on the intermittent plan, with iodides between the courses of arsphenamine and mercury. From the ophthalmic standpoint, the appraisal of the results of treatment is unsatisfactory, since the functional result depends on the accidental location of the opacity. Syphilitic keratitis does not exclude the use of the arsenicals, according to the author's experience in this series.

GRANULOMA INGUINALE: ITS OCCURRENCE IN THE UNITED STATES. H. FOX, J. A. M. A. **87:**1786 (Nov. 27) 1926.

Fox has collected 150 cases of the disease reported in this country. This includes fifteen cases of his own.

It is evident that the disease is more prevalent than the recorded cases indicate and that it is endemic in both the North and the South. The author's patients, with one exception, were negroes. There were nine males and six females. The average age was 26½ years. Donovan's bodies were found in eleven cases. Because of irregular attendance, treatment was unsatisfactory in most of the cases, but in three cases there was complete or almost complete healing, and in three others decided improvement. The patients were treated with tartar emetic. In one case the disease practically disappeared with roentgen-ray treatment alone.

SYPHILIS OF THE CERVIX. G. GELLHORN, J. A. M. A. **87:**1812 (Nov. 27) 1926.

This condition is not as rare as it is generally thought to be. Manifestations of each of the stages of the disease may occur on the cervix. They are described by the author.

In the differential diagnosis, several conditions present themselves, but cancer is the most important. In supposed cancer of the cervix, a syphilitic

therapeutic test is in order if there is the slightest doubt as to the true nature of the disease.

The author calls attention to the infectiousness of cervical secretions in a syphilitic woman, even though there is no demonstrable lesion of that structure. Syphilitic lesions of the cervix may give rise to dystocia, which becomes of great importance should the woman become pregnant. Syphilis of the cervix is also a predisposing factor in the development of cervical cancer. Three cases bearing on this association are reported. The author believes that more alertness toward syphilis of the cervix will remove it from the class of rare manifestations of syphilis.

MALARIA TREATMENT OF CENTRAL NERVOUS SYSTEM SYPHILIS. J. R. DRIVER, J. A. GAMMEL and L. J. KARNOSH, J. A. M. A. **87**:1821 (Nov. 27) 1926.

The authors report the results obtained by this method in sixty-five cases. Their method of malaria inoculation, number of chills allowed, and clinical and laboratory control followed that commonly employed.

In the group of thirty-one general paralytic patients, eight obtained complete remissions, and eight moderate remissions. The condition in four was slightly improved and in seven unchanged, while there were four deaths due to intercurrent infections.

Pronounced clinical improvement was seen in three cases of taboparesis, moderate or slightly improved in six and no change in four. There was little effect in two cases of juvenile paresis. Of twelve cases of tabes, in three there has been complete relief of severe lancinating pains; in four marked reduction in their severity was noted; while in four only slight or no improvement was obtained. Of seven cases of cerebrospinal syphilis, there was some improvement in the spinal fluid serology in five, while two patients escaped final observation.

This report is necessarily a preliminary one, but the authors consider that the results obtained warrant the employment of this form of therapy in selected cases of neurosyphilis which no longer show improvement by the usual methods of modern antisyphilitic treatment.

CHEMICAL ANALYSIS OF SWEAT: A FURTHER STUDY. R. E. BARNEY, J. A. M. A. **87**:1827 (Nov. 27) 1926.

Supplementing his earlier report, Barney reports the results of an investigation in seventeen normal persons, in five cases of senile eczema and in seven of psoriasis. The sweat was obtained by the injection of pilocarpine and a sweat bath between rubber sheets.

Under these conditions, uric acid was not found in a significant amount in any specimen. The cases of psoriasis showed no essential deviation from the normal, but in the group of cases of senile eczema there was a decided diminution in the output of nitrogenous elements and chlorides.

MICHAEL, Houston, Texas.

CHEMOTHERAPEUTIC EXPERIMENTS WITH COAL-TAR DYES ON SPONTANEOUS MOUSE TUMORS. B. T. SIMPSON and M. C. MARSH, J. Cancer Research **10**:50 (April) 1926.

Intravenous and subcutaneous injections of a therapeutic dosage, of seventy different coal tar dyes into albino mice with palpable spontaneous mammary adenocarcinomas failed to show inhibition of tumor growth.

IODINE IRRITATION DOES NOT PRODUCE CANCER. J. ROSENSTIRN, J. Cancer Research **10**:61 (April) 1926.

Two hundred albino mice susceptible to cancer received repeated localized applications of iodine preparations over a period of eighteen months. The only reactions observed were lymphocytic and fibroblastic infiltration.

CONCERNING GYE'S HYPOTHESIS OF THE ETIOLOGY OF MALIGNANT TUMORS WITH SPECIAL REFERENCE TO THE "SPECIFIC FACTOR." M. J. HARKENS, J. F. SCHAMBERG, J. A. KOLMER and C. M. KAST, J. Cancer Research **10**:66 (April) 1926.

For the production of cancer, Gye considers it necessary to have an interaction between an ultramicroscopic virus and an activating chemical substance. The latter, which he calls the "specific factor," is thought to break down cell defenses, rendering tissue liable to infection with the virus. The experiments carried out by Schamberg and his co-workers failed to show the production of Rous chicken sarcoma by the employment of "subculture" and "specific factor" except in those cases in which the control "specific factor" when used alone also produced a tumor. These investigators have shown that the production of experimental chicken sarcoma is dependent on the presence of a living virus in the "specific factor." When the virus in the "specific factor" was definitely inactivated, the experimental results were negative.

H. R. FOERSTER, Milwaukee.

SOME HISTORICAL AND CLINICAL REMARKS ON THE EFFECT OF LIGHT ON THE SKIN AND SKIN DISEASES. C. RASCH, Proc. Roy. Soc. Med. **20**:11 (Nov.) 1926.

Some of the earliest recorded experiments on the action of sunlight on the skin were performed by an English physician, Sir Everard Home (1763-1832). By covering part of the dorsal surfaces of the hands with cloth and recording the temperature beneath it and on the open surface, he found that on exposure to sunlight the temperature beneath the cloth was higher but that a dermatitis occurred on the uncovered portion, thus indicating the action of an actinic ray rather than heat. He further demonstrated the comparative resistance of pigmented skin to sunlight. Brief reference is made to other early contributions on the subject. Wilson (1798) first described a disease due to sunlight under the name of eczema solare. Xeroderma pigmentosum was described by Kaposi in 1870, but he did not at this time ascribe it to the action of sunlight. In 1878, Hutchinson described prurigo aestivalis. In 1906-1907, Dubreuilh stated that most of the epitheliomas of the face, together with the common so-called senile alterations of the skin, are produced by sunlight. In 1911, J. H. Sequeira described "permanent freckles," and in 1917, Riehl described the so-called war melanosis, the almost black pigmentation called forth by light. Bazin's hydroa and transitional types are mentioned. The author records 231 cases of hereditary light eruptions in 31,000 dermatologic cases in Denmark between 1911 and 1925. These included examples of polymorphous light eruptions (Rasch), hydroa vacciniformis (Bazin) and a special syndrome first described by Prof. T. McCall Anderson of Glasgow comprising porphyrinuria (congenital), large blebs with resulting ulceration and destruction of the nose and ears and lesions of the hands resembling sclerodactylia. Two cases each of xeroderma pigmentosum and Riehl's melanosis were seen and a histologic resemblance of the latter to lichen planus was noted. Colloid

milium and chronic dermatitis of the neck due to sunlight were seen as were also pigmented spots, achromic spots, atrophic macules, keratoses and epitheliomas due to light. It is recorded that smallpox will heal without scars if the patient is kept in the dark. Attention is directed to a group of diseases aggravated by light, such as rosacea and lupus erythematosus; acne vulgaris, secondary syphilitic eruptions, elephantiasis and lichen planus are mentioned as examples of conditions favorably affected by light. Thirteen illustrations and an extensive bibliography accompany the article.

GUY, Pittsburgh.

TROPHONEUROTIC GANGRENE OF THE SKIN. K. H. VOHWINKEL, Arch. f. Dermat. u. Syph. **152**:75 (Nov. 13) 1926.

Vohwinkel's patient, a man, aged 47, presented typical lesions of trophoneurotic gangrene of the skin of the face, of nine months' duration. Twenty-one years before, a revolver bullet had become lodged in the right temple, since which time he had noticed anesthesia of the right side of the face, diminished sense of taste in the right half of the tongue and a mist before the right eye. When the patient was examined for the gangrene, neuroparalytic dystrophy of the right eye and atrophy of the facial muscles on the right side were attested, as well as the taste interference noted above. The bullet was discovered in the right middle cranial fossa and removed, and one month later the necrotic lesions had all disappeared, except one on the lip, which was healing. Vohwinkel considers this case significant, as clearly bringing to light the connection between the nervous system and the skin phenomena of this disease, and as one of the rare observations in which trauma was a factor in the etiology. As an explanation of the sudden appearance of the symptoms after twenty-one years, he suggests some quick movement on the part of the patient, shifting the position of the projectile, which now set up an irritation of the right trigeminal nerve.

NECROSIS ADIPOSA NEONATORUM. G. GELBJERG-HANSEN, Arch. f. Dermat. u. Syph. **152**:91 (Nov. 13) 1926.

Gelbjerg-Hansen condemns the name scleroderma neonatorum for subcutaneous fat necrosis in the new-born, and proposes that given above. He affirms that this is a clearly demarcated and typical disease picture, which cannot be confused with any other. The etiology is unknown, but he suggests a pancreatogenous origin. In the case described by him, the disease made its appearance when the child was 4 days old, with dark red patches on the outer side of both arms and in the left infrascapular region. Apparently the entire thickness of the skin was infiltrated. In the course of the next eighteen days, similar infiltrations appeared on the right shoulder (the size of a child's hand), on the outer surface of each thigh (2 by 5 cm.), on the back over the angle of the left scapula and on the left hip (8 by 4 cm.). Thirty-seven days after the onset, the skin was found entirely normal, the infiltrations had disappeared and atrophy was not present. Microscopic examination of a portion of one of the infiltrated patches showed that the seat of the disease was the subcutaneous fatty tissue, the necrosis of which was accompanied by considerable inflammatory reaction. The general health of the affected infants does not appear to suffer and the skin lesions clear up without treatment. This is the first case described from Denmark. Twenty cases were found in the literature.

EXPERIMENTAL RESEARCHES ON THE ACTION OF SHORT-WAVE ULTRARED RAYS ON THE SKIN. W. JADASSOHN, Arch. f. Dermat. u. Syph. **152**:113 (Nov. 13) 1926.

Jadassohn made about twenty irradiations of normal human skin, treating a field 8 cm. in diameter in each case. When the intensity of the rays is slight and the time of irradiation brief, the reaction, consisting of an immediate erythema, extending beyond the field irradiated, disappears within the first hour, leaving a red spot corresponding exactly to the area treated. This spot also vanishes in from three to five hours. Sensibility is normal. When the intensity of the rays is greater and the time longer, a wheal, the size of the irradiated field, appears within a few minutes in the center of an area of erythema. Within the first hour the wheal develops into a blister, and the redness disappears. In the course of a few days the blister either breaks or dries up, and a small ulcer, covered with a crust, appears. This ulcer heals very slowly. Pain is absent throughout the course of the reaction. There is hyposensibility of the irradiated area. Microscopic studies were made at various periods of the reaction. An effect on the deeper tissues was not noted until several days after the irradiations. Investigations are being made on the action of ultrared rays on pathologic tissues.

HERPES ZOSTER FOLLOWING ROENTGEN IRRADIATION. H. T. SCHREUS, Dermat. Wchnschr. **83**:1606 (Oct. 30) 1926.

A boy, aged 11, received roentgen-ray treatment for Hodgkin's granuloma. Thirty-three per cent of the erythema dose was applied to the splenic region (200 kilovolts, 4 milliamperes, 0.5 copper filter, 30 cm. distance), and, with intervals of a day or so, to the left side of the neck and both sides of the thorax; the right side of the neck was given 20 per cent of the erythema dose. About forty days after the irradiation of the left side of the neck, the child developed severe herpes zoster in the region of the left second and third cervical ganglions. The lesions healed in fourteen days. Schreus believes this to be the first case reported in which herpes zoster has followed exposure to the roentgen ray. He thinks it probable that a latent zoster infection or tendency existed, which was brought into activity by the irradiation.

ZAPFFE, Chicago.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

EFFECT OF CUTTING ON RATE OF HAIR GROWTH. R. J. SEYMOUR, Am. J. Physiol. **78**:281 (Oct. 1) 1926.

Seymour has made personal observations of hair growth for nearly three years. He says that in some undetermined manner shaving serves as a stimulus to growth of facial hair in man; the actual cutting of the hair seems to be the accelerating factor. The rate of hair growth is most rapid immediately subsequent to cutting, the rate gradually lessening as the time of cutting becomes more remote. Although variations in rate were found, no correlation with temperature or season was noted. Apparently the hyperemic conditions that accompany shaving are not responsible for the acceleration of the growth rate.

TREATMENT OF HEMANGIOMA AT COLLIS P. HUNTINGTON MEMORIAL HOSPITAL. G. W. TAYLOR, Boston M. & S. J. **195**:737 (Oct. 14) 1926.

One hundred and ninety-three cases of hemangioma are described and analyzed by Taylor. The results of surgical treatment are given. The technic of radium treatment and the results secured with it are discussed. Surgical excision is the method of treatment preferred in small accessible hemangiomas when a scar will not be disfiguring. Radium treatment is successful in telangiectatic angiomas and in small superficial lesions of the skin or mucous membranes. Radium treatment is moderately satisfactory in deep seated lesions. Radium treatment is unsatisfactory in port wine marks and in superficial diffuse lesions. Reactions with their sequelae of scars and telangiectases can largely be avoided by using only silver screened radiation.

VASCULAR REACTIONS OF SUSCEPTIBLE SKIN TO PROTEIN. R. HARE, Heart **13**:227 (Sept. 29) 1926.

Experiences bearing on the irresponsiveness of the minute vessels of the skin are described by Lewis, and observations on a number of chosen clinical cases are reported. It is shown that the vessels of the skin which had been injured in a number of ways, by stroking in the susceptible, freezing, burning, the application of mustard gas, or irradiations from a mercury vapor lamp, are subsequently dilated and the skin becomes more or less edematous. When the edema has subsided, these vessels are found to be in a peculiar condition. They contract imperfectly to the stimulus of epinephrine hydrochloride and pituitary extract, or refuse to contract at all. They are more or less refractory to the stimulus of histamine. A case of erythema ab igne is described, in which the vessels of the affected skin entered the same peculiar state. Several cases of telangiectasis arising out of known injuries, and several arising from unknown causes, are described. The vessels involved vary; in some, the superficial venules are alone dilated; in others, the capillaries are also involved. Two patients with congenital nevus are similarly examined. In all these cases the affected vessels are found to be more or less irresponsive to vasoconstrictor substances and to histamine. The same statement applied to diffuse telangiectasis of the weather-beaten face and to leashes of venules on the chest wall. It is argued that the vessels comprising telangiectases (and congenital nevi) have become dilated because they have lost their contractile power; and that the peculiar condition of these vessels is similar to or identical with that which occurs immediately or soon after actual injury.

INTRADERMAL VACCINATION AGAINST SMALLPOX. M. BUSSEL and R. STANKIEWICZ, Rev. franç. de Pédiat. **2**:293 (July) 1926.

Bussel and Stankiewicz vaccinated 683 children at Warsaw by intradermal injection of the vaccine, and commend this technic (Leiner) as safe, effectual and convenient. It is indicated especially for children with the exudative diathesis, tuberculosis or chronic skin disease, and during epidemics, even in acute dermatoses. There is no chance for infection of the eyes, or of other children, and there is no ugly scar. They found the preferable technic an injection of 0.1 cc. of animal vaccine diluted 1:80. The needle is inserted in the germinative layer of the epidermis, for from 0.5 to 1 cm. A control injection of physiologic sodium chloride solution is made in the other arm. The specific reaction developed the fifth or sixth day, reaching its maximum about the twelfth, with redness and hard infiltration; in a few cases a minute vesicle

formed. The children did not feel sick; the course of the vaccinia was attenuated, but at its height there was some fluctuation of temperature. The glands in the axilla were slightly enlarged in some of the children. In seven cases local suppuration and necrosis developed, ascribed to inadequate dilution (1:40); three in this group were of lymphatic type, and the injections had been made too close to the surface.

ARSPHENAMINE THERAPY. H. T. SCHREUS, Arch. f. Dermat. u. Syph. **150**:402 (July 1) 1926.

Schreus injected vital dyes or arsphenamine compounds subcutaneously or intravenously into experimental animals (mice and rabbits) and studied the relations between the concentration of doses and the distribution in the body. The main thing in improving the action of arsphenamine is to attain a saturation of the body. By breaking up the dose it is possible to obtain this at the same time that the arsphenamine concentration of the blood is kept low. The results of his clinical studies, comprising seventy-three cases, show that regularity and sufficient number of arsphenamine injections, at least ten, in combination with mercury or bismuth are of the greatest importance. Improvement in arsphenamine treatment can be made by increasing the size of the single doses, by prolonging the treatment or by combining arsphenamine with substances acting as vehicles.

SYPHILIS AND ACUTE YELLOW ATROPHY OF THE LIVER. A. NEDDERMEYER, Arch. f. Dermat. u. Syph. **150**:423 (July 1) 1926.

Neddermeyer presents eight fatal cases with the clinical diagnosis of acute yellow atrophy of the liver, with simultaneous syphilis in six cases. He indicates that the atrophy of the liver did not depend on arsenic poisoning due to the arsphenamine treatment. The explanation is a specific toxic effect of the syphilitic infection on the liver cells, without a direct action of the spirochetes.

DETOXICATED ARSPHENAMINE. E. S. HERONIMUS, Arch. f. Dermat. u. Syph. **150**:459 (July 1) 1926.

In experiments on twenty-nine mice inoculated with Dutton's spirochetes Heronimus found that arsphenamine, detoxicated by serum in vitro, did not lose its sterilizing power. In 86 per cent a complete sterilization was obtained. The detoxicated substance had the same effect as arsphenamine dissolved in water or physiologic sodium chloride solution.

ACTION OF AMIDOPYRINE ON GENITALS. E. LASCH and A. PERUTZ, Arch. f. Dermat. u. Syph. **150**:474 (July 1) 1926.

Lasch and Perutz studied the effect of amidopyrine on the uterus and spermatic cord of rats and guinea-pigs. They found that the drug decreased the tonus and had a quieting effect on the organs. They conclude that the clinical effect of amidopyrine on the smooth musculature of the genital tract is not only central but also peripheral.

Society Transactions

ST. LOUIS DERMATOLOGICAL SOCIETY

Regular Meeting, October, 1926

ROBERT H. DAVIS, M.D., *in the Chair*

PROGRESSIVE PIGMENTARY DERMATOSIS (SCHAMBERG'S DISEASE). Presented by DR. GAROLD V. STRYKER.

Mr. M. J. B., aged 35, was presented because of a condition of ten years' duration which began on the lower third of the right leg, spreading slowly until the skin of the foot and ankle was involved. The active border was made up of from "pin-point to pinhead" sized, reddish puncta, closely resembling grains of cayenne pepper. On the ventral surface of the ankle and over the internal maleolus were reddish brown patches, measuring from 5 to 6 cm. in diameter. The older areas on the lower part of the leg had lost their telangiectatic appearance and were brownish yellow. Areas of atrophic changes could be made out.

DISCUSSION

DR. R. H. DAVIS: The only question is whether the condition is Schamberg's disease or Majocchi's disease. They are so much alike that they are often confused one with the other. Possibly an absolute diagnosis could be made from a histologic examination. I think the case is one of Schamberg's disease. The annular configuration, which is so often seen in Majocchi's disease, is not present in this case.

DR. TOOMEY: Is there any essential difference between the two diseases, Schamberg's and Majocchi's? I do not think so.

DR. DAVIS: Majocchi's disease is said to have little cell infiltration while Schamberg's has marked infiltration, especially near the sweat ducts.

DR. TOBIAS: As I understand it, most vascular cutaneous conditions of the lower extremities are due to the same causes, there being an anatomic difference in the distribution of the veins and in the condition of their walls.

PEMPHIGUS CHRONICUS. Presented by DR. ERICH BROCKELMANN.

A young man, aged 18, gave the following family history. His father died at the age of 55 from apoplexy; he had had psoriasis. His paternal grandmother also had psoriasis. His mother had diabetes mellitus and hemophilia. An aunt also had hemophilia. The patient was vaccinated at the age of 2½ years. He had had measles, mumps and chickenpox, and at the age of 13 had suffered frequent attacks of follicular tonsillitis. When he was 12 years old, he had had the first attack of pemphigus on one leg. Blisters appeared in successive crops at irregular intervals about every second year, each crop lasting for two or three weeks, the bullae being confined to the lower limbs and forearms. These attacks usually began in June, disappearing in the fall. There was little pruritus. Since 1925 the patient had had boils at infrequent intervals. Three weeks before presentation he had had what he described as "poison ivy" on both forearms, a number of small, pruritic vesicles which

disappeared about one week after their onset. At presentation the patient had a healthy appearance. Several unilocular bullae, varying in size from that of a pea to that of a cherry, were observed on both legs. Only the large ones showed a halo surrounding them. The bullae were hard and tense, becoming flaccid when enlarged. They contained a clear, yellow fluid. When ruptured they left a raw, oozing surface, covered with yellowish serous crusts and the loose epidermis. The patient has been under the "Davis" treatment.

DISCUSSION

DR. GREINER: I think the condition is chronic pemphigus.

DR. STRYKER: I agree.

DR. TOBIAS: I consider it difficult to make a positive diagnosis of pemphigus. I would suggest epidermolysis bullosa.

DR. BROCKELMANN: The Nikolsky test was negative. The family history is of especial interest, psoriasis having been reported in the father's family and diabetes mellitus and hemophilia in the mother's family.

DR. DAVIS: The condition is more probably pemphigus, as the lesions arose from the sound skin and were not accompanied by pruritus. Such symptoms would indicate pemphigus, impetigo or epidermolysis bullosa, but in this patient there was no condition suggestive of epidermolysis bullosa, and it was evidently not impetigo. The absence of pruritus would also exclude dermatitis herpetiformis. I think the condition will develop into a case of true pemphigus.

DR. TOOMEY: I agree.

HEREDITARY HEMORRHAGIC TELANGIECTASIS. Presented by DR. G. V. STRYKER.

Four years ago, Miss E. K., aged 26, noticed a mottling of the cheeks and chin. This mottling had continued. From a distance it appeared as a blush over the cheeks, on the nose, along the ramus of the mandible and on the chin. On close inspection multiple capillaries in the epidermis were observed. The patient had had measles, chickenpox, acute rheumatic fever and frequent sore throat. She said that she had had severe "nosebleeds" since early childhood which continued until five years ago. At the age of 9, she had a severe hemorrhage from the nose which persisted for three days. At 17, she had at times two hemorrhages a day, extending over a period of several days. Menstruation began at 15, and has been regular and of moderate amount, attended by severe dysmenorrhea. Wounds have always bled profusely and the bleeding is stopped with difficulty.

DISCUSSION

DR. TOBIAS: I think the condition is a telangiectatic rosacea because of the limitation of the condition to the flush areas of the face, its symmetry of outline and the history of succeeding attacks of flushing of the face before the telangiectatic condition presented itself.

DR. STRYKER: The case was presented as "hereditary telangiectasia" because of the telangiectatic condition over such an extensive area with a duration of a number of years, in accordance with a case reported by Williams in 1926. Each case reported had a history of hemorrhage of the nose extending over a considerable period of time, also a history of heredity.

DR. DAVIS: I agree with Dr. Stryker, but suggest further observation for verification of this diagnosis.

DR. TOOMEY: I do not consider the condition hereditary hemorrhagic telangiectasis as described by Osler about 1893. I believe this case is a telangiectasis of thyrotoxic origin. It is interesting to note that Dr. Osler's description was not the first description of this disease but that he had been anticipated some six years before by a little known writer whose name I cannot recall.

DR. DAVIS: These conditions are in some cases "spider naevi," in others telangiectases, in others plaques (nevi that are small and slightly raised). A case may be characterized by only one of these types, or by more than one, as mentioned by Williams (ARCH. DERMAT. & SYPH. **14**:1 [July] 1926).

CONGENITAL SYPHILIS. Presented by DR. E. R. SEALE (From the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook).

C. S., a boy, aged 5 weeks, was presented because of a condition which began three days before with lesions on one arm and on one leg and had since spread over the entire body. The child's mother had been married two years. She had had one miscarriage fourteen months before. There was no history of primary lesion or of generalized eruption. The patient presented a universal eruption on an erythematous skin, made up of three distinct types of lesions: 1. On the extremities and face there were rather deep-seated vesicles, varying in size from 0.25 to 0.5 cm. in diameter, some of which were excoriated and crusted, those on the face being more superficial with superimposed crusts. Others were pustular in character, particularly on the forearms. 2. On the body the skin was erythematous, and the predominating lesions were small red papules. 3. Scattered over the body, especially on the posterior aspect of the thighs and buttocks, were distinct, rather bright red wheals, varying in size from 0.5 to 2 cm. in diameter. The palms and soles showed nothing but the aforesaid erythematous process. The Wassermann reaction was negative.

DISCUSSION

The consensus of opinion was that the condition was congenital syphilis

A CASE FOR DIAGNOSIS. Presented by DR. E. R. SEALE (From the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook.)

J. M., a white man, aged 43, had had a mole on the leg all his life. A few years ago the patient scratched it, and it began to grow from its surface. For the last few weeks before presentation it had been discharging pus. On the posterior aspect of the middle third of the right leg there was a circular lesion, about 3 cm. in diameter, slightly indurated. The outer portion was dusky red and the center brighter red and raised above the surface. The latter was about the size of a cherry, fairly firm and discharging purulent material. The diagnosis seemed to lie between granuloma pyogenicum and sarcoma. The condition was treated as an infected lesion, using hot boric packs. After ten days the lesion was noticeably smaller, and practically all infection had disappeared.

DISCUSSION

DR. DAVIS: Judging from the history of the lesion, I think it is malignant, with a secondary pus infection. When first observed, it suggested granuloma pyogenicum, but at this time I would offer no definite diagnosis.

A Case for Diagnosis. Presented by Dr. E. R. Seale (From the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook).

C. H., a white man, aged 35, had an acute dermatitis of five months' duration, in the left axilla, which had become generalized within three weeks. There had been no internal medication. A general physical examination revealed soft systolic murmurs at both the aortic and the mitral areas. The blood pressure was 124 systolic, 58 diastolic. There was generalized lymph adenopathy, edema of the feet and ankles and no splenomegalia. The skin presented a universal dry, scaly condition with exfoliation to a moderate degree. The skin was thickened, especially in the palms. The red blood cells numbered 5,500,000; white blood cells, 21,200; hemoglobin, 85 per cent; lymphocytes, 37 per cent; transitionals, 3 per cent; eosinophils, 8 per cent; polymorphonuclears, 52 per cent. Urinalysis revealed nothing pathologic.

DISCUSSION

Dr. Davis: I would diagnose the condition as a type of leukemia cutis.

Dr. Greiner: I agree with Dr. Davis.

Dr. Brockelmann: I think the condition resembles arsenical keratosis.

Dr. Toomey: I do not think there is sufficient evidence to make a positive diagnosis of leukemia cutis at present. What the toxin is, I cannot say, but the pronounced adenopathy in the right inguinal gland is suggestive of a leukemia cutis. Even the latter, however, may occur in exfoliative dermatitis as a result of arsenical or any other intoxication.

Norman Tobias, M. D., Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 12, 1926

Rose Hirschler, M.D., *Presiding*

Extensive Multiple Epitheliomas Resembling Psoriasis. Presented by Dr. Pfahler.

Mr. B. S., aged 57, was referred with the diagnosis of psoriasis of eight years' duration. Four years before examination, he received roentgen-ray treatment over the hands and the posterior left axilla. He developed a radio dermatitis over both hands and the left axilla, and in addition had a radiation ulcer in the axilla. Electrocoagulation was followed by skin grafting in the axilla. At presentation there was an epithelioma growing over the second joint of the left ring finger, and the whole outer side of the second phalanx was diseased. The epithelioma was elevated about 1.5 cm. and was approximately 1.5 cm. in diameter. An epithelioma about 3 cm. in diameter was seen at the edge of the scar in the posterior left axilla, and many epitheliomas were scattered over the body. These varied in size from 1 to 5 cm. in diameter. They were covered with scales, some elevated only 1 or 2 cm. They resembled closely psoriasis, but had more induration than is found in psoriasis. Two small untreated lesions, which had the appearance of psoriasis, were resected for microscopic study, and these were reported to be basal cell epitheliomas.

DISCUSSION

DR. CASE: The lesion was small and thin, with little or no hyperkeratosis. At one spot there had been an exudate beneath which there was a definite early basal cell carcinoma. In one or two other places there was a tendency to grow downward. In the upper layers of the corium there was a dense infiltration composed of mononuclear leukocytes.

DR. PFAHLER: I doubt whether the former diagnosis of psoriasis was correct. Such a mistake is easily made. I do not think the lesions could be due to roentgen ray, as application of radiation was made to three areas only.

DR. WERTHEIMER: I think the condition clinically is similar to Bowen's disease, in which it is difficult to make an early diagnosis. The lesion on the right foot is typical.

DR. SCHAMBERG: This condition is not uncommonly seen in persons who have a cutaneous tendency toward these changes. Electrodesiccation is the best treatment, though for the superficial lesions, carbon dioxide snow can be used with benefit.

DR. CRAWFORD: I agree that in multiple basal cell carcinoma, electrocoagulation is indicated.

DR. WEIDMAN: The uniformity of the infiltration, both as to distribution as a whole and as to individual cells in the corium, leads me to believe that there is something underlying the changes, for I have never seen such uniformity in ordinary epithelioma.

DR. GREENBAUM: In all probability a certain number of the lesions will show the kind of cells found in Paget's disease of the nipple, and some will show the kind of cells found in Bowen's precancerous dermatosis.

NOTE: Subsequent histologic examinations have shown that the ulceration in the scar of the surface of the left axilla was a squamous cell carcinoma, type 1, and the epithelioma of the left ring finger was a combined basal cell and squamous cell carcinoma.

EPILATION OF HALF THE SCALP IN A PATIENT WITH STRAIGHT HAIR, FOLLOWED BY A REGROWTH OF CURLY HAIR. Presented by DR. PFAHLER.

Mrs. J. S., aged 47, was treated first on July 20, 1925, on account of advanced carcinoma of the right breast, associated with extensive metastases. Metastatic carcinoma of the left cervical region, in 1925, had caused complete palsy and much pain in the left arm. By May 7, 1926, the diseased area was recalcified, and the use of the left arm was recovered. On March 5, 1926, metastasis was discovered in the anterior half of the left side of the skull. Treatment was then given with high voltage roentgen rays, resulting in complete recalcification of the diseased area. The treatment caused a complete epilation on the left side of the scalp. On October 8, the patient had a heavy regrowth of hair, approximately 1 inch (2.5 cm.) long, of the same color as that on the opposite side (dark red, or titian), but on the treated side, the hair was now curly, whereas on the untreated side it was straight.

ARSENICAL DERMATOSIS. Presented by DR. QUINLAN for DR. SCHAMBERG.

Mr. T. S., aged 26, gave a history of itching skin of eight months' duration. This followed an infiltration of arsphenamine into the arm. The skin over the body was dry, scaly and indurated, with much pigmentation. All laboratory tests gave normal reactions. He was given 5 cc. of thiosinamine intravenously, with complete relief from the itching.

DISCUSSION

DR. GREENBAUM: The patient has had the arsphenamine dermatitis for eight months. It is the type that lasts a long time, seen particularly in the colored race. He is presented to demonstrate the fact that in a certain percentage of cases in which there is pruritus, thiosinamine will give quick relief — within eight hours. In 75 per cent of the cases relief is experienced. The dose is 3 grains (0.2 Gm.) intravenously, given slowly. It consists of 3 grains (0.2 Gm.) in a 2 per cent solution of glycerin, aqueous solution. There is a bad taste after administration, but no other ill effects.

DR. SCHAMBERG: I have seen cases in which there was definite improvement. The sulph-hydroxyl group seems to have a favorable effect in controlling the metallic eruptions.

DR. KLAUDER: Has any one used other sulphur preparations? In Germany calcium is used in the treatment of an arsphenamine dermatitis.

A CASE FOR DIAGNOSIS. Presented by DR. QUINLAN for DR. SCHAMBERG.

Mr. C. G., aged 29, was admitted to the Polyclinic Hospital in March, 1920, with chronic gonorrhea. On September 14, reaction to the gonococcus fixation test was negative. He was readmitted October 16, on account of varicose veins of the legs. These were excised. The history showed that his mother died of tuberculosis. He had had typhoid fever at the age of 15, but otherwise had been healthy. In 1916 while doing heavy work his "legs gave out under him," but treatment was administered and he recovered. Some time later the condition recurred, with much pain in the thighs and legs. There was some edema of the legs. Examination of the heart, lungs and abdomen gave negative results.

He was readmitted, Oct. 21, 1921, with swelling of the veins in the arms, thighs and legs. Small, deep-seated nodular lesions were present along the course of the veins. These were, and are at present extremely tender. Otherwise, the entire physical examination including stomach analysis and gall-bladder drainage, gave negative results. A diagnosis of thrombophlebitis migrans was made at that time.

The condition has not changed — the swollen veins on the legs and the tender knots on the veins are still present.

DISCUSSION

DR. STOKES: The condition resembles a papulonecrotic tuberculid. Some of the lesions are nodose subcutaneous swellings, with central necrosis. Possibly it is simply a nodose lesion associated with chronic infections of other types.

DR. WEIDMAN: I agree with Dr. Stokes as to the basic considerations in the case. This particular expression has been described in England as "fibrositis." The extreme sensitiveness is a part of it as described, and the condition is supposed to be due to chronic focal infection of various types.

DR. SCHAMBERG: The history is unusual for papulonecrotic tuberculid. The patient has been suffering for five years with acute attacks, and the nodules seem subcutaneous, rather than cutaneous. The extreme tenderness and the acute attacks are not seen in the papulonecrotic tuberculid.

DR. GUY: I think that the lesion is an infectious process, subcutaneous — perhaps a rheumatic nodule.

DR. STOKES: The condition belongs in the group of vascularly distributed infections, with a nodule which sometimes undergoes necrosis — not necessarily due to the tubercle bacillus.

DR. HOLLANDER: The marked hyperhidrosis on the palms may have some relation to the hypersensitiveness of the hands.

DR. GREENBAUM: The consensus of opinion is that the lesions are due to multiple emboli. However, a diagnosis was not made, after a thorough examination, which revealed only a prostatitis.

TUBERCULOSIS CUTIS. Presented by DR. PFAHLER.

F. B., aged 42, a colored, trained nurse, three years previously developed a small blister on the right elbow. She was nursing a tuberculous patient and, at the same time, a patient with syphilis. The Wassermann reaction was negative four times, and two roentgenograms did not show any evidence of pulmonary tuberculosis. Biopsy revealed that the lesion had the appearance of tuberculosis, but bacilli could not be demonstrated. Nine one-fourth unit doses of the roentgen ray were administered at weekly intervals, and three one-half unit doses at fourteen day intervals, without improvement. The ulceration is now irregular, measuring 4 cm. in width, 2.5 cm. in height and probably 4 mm. in depth, with a somewhat thickened base. Under all circumstances, it would seem advisable to destroy the disease by electrodesiccation, and then, during the process of granulation, to follow with roentgen-ray treatment in one-half units, with 9 by 5 by 5, 20 cm. distance, 2 mm. filter, equaling approximately one half of the erythema dose. The patient has pigmented scars elsewhere about the elbow, equaling about twice the area of this ulcer.

DISCUSSION

DR. GUY: I think the condition may be tertiary syphilis.

DR. SCHAMBERG: The condition may be either tuberculosis or syphilis. The appearance was modified by the roentgen rays. A negative Wassermann reaction is not sufficient evidence of the absence of syphilis; therefore, antisyphilitic treatment should be given. The introduction of the Wassermann test has caused many physicians to omit therapeutic tests when there is a negative Wassermann reaction. I do not submit to either diagnosis.

DR. STOKES: The condition is probably syphilis.

A CASE OF TUBERCULOSIS. Presented by DR. PFAHLER.

Mr. A. B., aged 43, was seen in May, 1925, with an ulceration of the lip which was due to irritation by a broken tooth. The tooth was extracted, but the ulceration continued. A diagnosis of epithelioma was made, and in spite of electrocoagulation, the disease continued. In May, 1925, it involved the left two thirds of the upper lip, with thickening three times normal, and the ulceration involved the entire inside of the left cheek. There were enlarged lymph nodes. The patient was given maximum radiation, which was kept at the point of saturation for two weeks. On September 8, only about one third of the disease remained, but the induration involved the cheek. Excision was advised, the surgeons agreeing. In February, 1926, the induration had almost entirely disappeared, but there was still a papilloma at the left corner of the lip. The skin was removed, and the disease destroyed. Microscopic examination showed it to be tuberculous. This was followed by two doses of the roentgen ray, 60 per cent each, which brought about complete healing of the disease about the mouth.

The patient was examined for tuberculosis of the lungs, and lesions were found throughout the upper two thirds of both lungs. Three months ago hoarseness developed which has not improved under treatment. The epiglottis was swollen, and there was scarring on the left anterior surfaces of both arytenoids, with swelling and edema. The left vocal cord was ulcerated. Both false cords were swollen and edematous. The posterior end of the right true cord was ulcerated. The patient cannot speak above a whisper.

In this patient, the tuberculosis of the mouth responded to radiation and electrocoagulation, while the tuberculosis of the lungs and larynx has not responded to general treatment. It is proposed to give stimulating doses of the roentgen ray over the lungs and the larynx.

Tuberculosis Cutis with Probable Mediastinal Tuberculous Adenitis. Presented by Dr. Pfahler.

J. H., aged 16, had a series of ulcers involving the subcutaneous tissue of the right axilla, extending down approximately 16 cm., involving also the infraclavicular and supraclavicular regions on the right side. There was a small ulceration just above the crest of the right ilium. A roentgenogram of the chest showed an abnormal mediastinal shadow overlying the shadow of the heart, and extending as high as the arch of the aorta. It also extended below, or to about the level of the diaphragm. Both the lateral and the anterior plates of the dorsal spine showed no evidence of disease of the vertebrae. It was thought at this time that the patient had an adenopathy, and that the condition inside the chest was definitely connected, and a part of the same process as that seen on the skin. He received one fourth of an erythema dose of roentgen rays, filtered through 6 mm., over all the lesions, five such treatments being given over each lesion. The response was satisfactory. The patient was first seen June 14, 1926, and the posterior lesions are now entirely healed. There was a gain in weight from 103 to 110 pounds (47 to 50 Kg.).

A review of the roentgenograms of the chest showed no evidence of pulmonary tuberculosis, but there was an abnormal mass in the mediastinum lying back of the heart, extending approximately 12 cm. above the diaphragm, and about 8 cm. below the diaphragm. It was fusiform in shape and had the general appearance of a tubercular sac, such as is found in cases of tuberculosis of the spine. The lateral view showed an abnormal infiltration involving the lower half of the mediastinum. There was definite disease between the ninth and tenth, and tenth and eleventh dorsal vertebrae, and apparently slight erosion on the anterior surface of the tenth and eleventh dorsal vertebrae.

Blastomycosis. Presented by Dr. Chambers for Dr. Stokes.

J. L., aged 24, a colored laborer, developed a lesion at the site of a glandular incision, in March, 1924. The incision failed to heal, and a verrucose growth appeared at the border of the incision. The growth progressed, enlarging peripherally, with a tendency to heal in the center. The past history was negative, except for chancre in 1920, and gonorrhea in 1925. The blood Wassermann test, blood count and differential count and urine test gave negative results. Biopsy of the lesion showed typical blastomycosis, and microscopic examination of the pus from the lesion revealed blastomycetes.

The treatment used consisted of Lugol's solution locally, sodium iodide intravenously and applications of the ultraviolet lamp and the roentgen ray.

DISCUSSION

DR. WEIDMAN: The classic picture was shown at biopsy, and the organisms were found repeatedly in the pus, though there was no growth in a culture. The yeast cells did not germinate. This is the first case of blastomycosis shown to the society in the last nine years. The old treatment consisted of curettage.

NOTE.—A subsequent culture has been successful.

DR. STOKES: I think this is a typical case of blastomycosis, though tuberculosis verrucosa cutis and epithelioma must be considered in the differential diagnosis. There is a variation in the response of blastomycosis to the iodides —sometimes 1,500 grains (97 Gm.) a day has been given with little influence on the lesion. Trauma should not be done to the lesion because the capacity for dissemination is poor.

DR. SCHAMBERG: Blastomycosis is rare in the eastern section of the United States. It is impossible to make the diagnosis purely on clinical grounds. Bromoderma may closely resemble blastomycosis.

ACRODERMATITIS PERSTANS. Presented by DR. KLAUDER.

A woman, aged 30, had been presented before the society previously. She had been treated with autogenous vaccines, of pure culture of *Staphylococcus aureus*, with definite improvement. It is consistent with the reports of others that if *Staphylococcus aureus* is present in pure culture, the treatment by autogenous vaccine is favorable. Many attempts at culture resulted in sterile growth.

DISCUSSION

DR. STOKES: Any improvement is a cause for congratulation, but the patient is still far from well, though the condition is not as hopeless as when she was shown before.

DR. GREENBAUM: A patient with a case not as extensive as this one was treated and cured with vaccines of *Staphylococcus aureus* obtained in pure culture.

DR. SCHAMBERG: The therapeutic result is gratifying. From time to time varying expressions of localized pyogenic infection of the skin are seen, and they often clear up under the use of vaccines, when they will not yield to anything else.

DR. WERTHEIMER: In a similar case of my own, the same infection seemed to attack the nails and the eyelashes.

DR. KLAUDER: Many negative cultures were obtained, and finally a special medium was used. In most of the cases cultures of *Staphylococcus aureus* have been obtained.

A CASE FOR DIAGNOSIS. Presented by DR. GREENBAUM.

J. B., a white boy, aged 15, when first seen some months ago, had exuding eroded areas on both the hands and the feet. They began as blebs on the backs of the hands and the soles, and between the fingers and toes. These burst, spread, cleared up and reappeared. Itching was intense. Continuous applications of permanganate seemed to cause the lesions to disappear. The patient was presented for suggestions as to further treatment and as to the etiology of the condition.

DISCUSSION

DR. CRAWFORD: I regard the condition as a chronic type of staphylococcia.

DR. WEIDMAN: I would suggest the use of gentian violet. The French are prone to regard impetigos as falling into two classes: those amenable to mercurial salts, and those amenable to gentian violet.

CONGENITAL ICHTHYOSIFORM ERYTHRODERMA. Presented by DR. CHAMBERS for DR. STOKES.

J. V., a white man, aged 18, Polish, was admitted to the hospital on Sept. 12, 1926. When he was 6 months old he had a generalized eruption consisting of small vesicles and papules. Crusting and scaling were prominent features at that time, according to his mother. This condition lasted for three or four months, disappeared and shortly recurred. Three years previous to the present attack, the patient was entirely free from cutaneous lesions. The present attack is of one year's duration. He also has arthritis of six months' duration, in which the onset was sudden, with chills and fever.

The urine was normal. The blood chemistry was negative. Examinations of the stool gave negative results. The blood Wassermann reaction was negative. The basal metabolism rate was plus 16. Prostatic secretion showed a moderate amount of pus. Roentgenograms of the knee showed slight atrophic changes. The blood count revealed: hemoglobin content, 90 per cent; erythrocytes, 4,320,000; leukocytes, 4,500—53 per cent polymorphonuclears, 40 per cent lymphocytes, 2 per cent large mononuclears and 5 per cent eosinophils.

DISCUSSION

DR. GUY: I think that the condition is due to concealed infection in the body.

DR. STOKES: The endocrine appearance of the boy fits in with that in cases of congenital ichthyosiform erythroderma. In those cases there are intermittent periods of good health. However, I would make no definite diagnosis.

DR. SCHAMBERG: I do not know whether the condition is ichthyosis, but I am inclined to agree with Dr. Guy, that there is an underlying common cause of the joint changes, and the skin condition. This cause may be endocrine.

DR. GREENBAUM: If the history is correct, the condition could well be ichthyosiform hyperkeratosis.

DR. STOKES: Ichthyosis and congenital ichthyosiform erythroderma do not look alike at all. Dr. Guy's suggestion was to the point.

DR. WEIDMAN: In the sections taken from one of the smaller nodules, the appearance was definitely not that of psoriasis or seborrheic dermatitis, as considered for a time, but it was that of a nondistinctive diffuse dermatitis. The distinctive histology of ichthyosiform hyperkeratosis was not present.

The fusiform, clubbed fingers of the patient should be noted, as well as the flat chest; these, together with the extreme arthritis of the knees, make the case a true hypertrophic pulmonary osteo-arthropathy, which has a tuberculous basis in such a large proportion of cases. Striae across the knees such as were seen in this patient had been mentioned in the literature in connection with calcareous metastases and osteocartilaginous changes, such as may be seen in destructive bone diseases, including tuberculosis. While there are one or two

breaks in the evidence and line of reasoning, if this case should be proved to be tuberculous, recalling the debated relationship of Hodgkin's disease to the tubercle bacillus, it is not a great error to regard the cutaneous changes as paratuberculous—something like those in Hodgkin's disease.

A Case for Diagnosis. Presented by Dr. Chambers for Dr. Stokes.

F. W., a colored man, aged 23, a laborer, for the last two years had had a papular eruption on the face, which did not trouble him. One month before admission he noticed some new lesions which appeared on the face, and which he termed "white spots." Shortly afterward, the scalp became involved, with a generalized papular eruption. The papules were heavily crusted. The patient complained of a diffuse tenderness of the scalp. The axillae were next involved with a papular eruption, and following this similar lesions appeared in the pubic region and the nuchal area. On admission, he complained of moderately severe pruritus in the pubic region, slight burning and lachrimation of the eyes, a sore mouth and generalized weakness. Two weeks after admission a moderate conjunctivitis appeared, with a discharge. The scalp, meanwhile, had progressed to a stage of moderate sloughing, accompanied by a marked foul odor. The past history was negative. The patient denied having had a primary lesion, but admitted having had gonorrhea three months before admission.

The laboratory observations were: urine — negative, except for the consistent presence of many hyaline casts; blood — hemoglobin content, 99 per cent; red blood cells, 5,000,000; color index, 100 per cent; leukocytes, 8,100; 40 per cent polymorphonuclears; 55 per cent lymphocytes; 4 per cent large mononuclears; 1 per cent eosinophils. The blood chemistry was normal. The blood Wassermann reaction was negative three times. Cultures from the hairs and crusts were negative. Biopsy showed edema and acute diffuse dermatitis.

DISCUSSION

Dr. Weidman: I would make a diagnosis of lichen scrofulosorum, associated with secondary syphiloderm.

Dr. Schamberg: The different elements of the picture are so divergent that they might be different dermatoses. The follicular keratotic patches do not look unlike syphilis, but they also resemble lichen scrofulosorum, although that is rare in a healthy adult. The most likely diagnosis is seborrheic dermatitis, with different expressions on different surfaces — moist in the axilla and scaly on the scalp.

Dr. Klauder: I think the condition most probably is a seborrheic eczema.

Trichotillomania. Presented by Dr. Schildkraut.

K. L., a boy aged 7 years, had spots on the scalp, first thought to be alopecia. On further study, the condition was found to be due to trichotillomania. The mother had a positive Wassermann reaction.

Linear Nevus. Presented by Dr. Schildkraut.

J. F., a boy, aged 14, three years ago developed a scaly, papular eruption, from the knee down to the tip of the great toe. The condition is still present. It was presented as a case of linear nevus.

PITTSBURGH DERMATOLOGICAL SOCIETY

Thirty-Eighth Regular Monthly Meeting, Oct. 21, 1926

FRED M. JACOB, M.D., *Presiding*

GRANULOMA ANNULARE. Presented by DR. WERTHEIMER.

Mrs. E. S., aged 42, for the last eighteen months had had a penny-sized, white, glistening, ring-shaped patch, with a firm nodular border, over the bridge of the nose. The entire mass was transversed by dilated capillaries, and the lesion was painful to pressure. When first seen about nine months ago the lesion was bluish red and somewhat crescentic. It began as a freckle about two years ago and has gradually enlarged. Local application of acid failed to change the course of the lesion. About November, 1925, the lesion was thoroughly curetted under procaine hydrochloride, and massive doses of the roentgen ray were applied.

DISCUSSION

DR. BEINHAUER: I believe the lesion is a basal cell epithelioma because of the age of the patient, the location of the lesion and the character of its border, which is definitely nodular, each nodule appearing as a definite epithelial pearl.

DR. HOLLANDER: The diagnosis of basal cell epithelioma was most evident, and I would treat the condition as such, using desiccation or electrocoagulation methods.

DR. BUSMAN: The lesion was raised, inflammatory and recurrent in type, and in spite of the intensive roentgen-ray treatment, I favor the diagnosis of a basal cell epithelioma or a granuloma of infectious character.

DR. WERTHEIMER: When I first saw this case I thought of epithelioma, keloid and granuloma annulare. On curettage I found the material extremely hard and resistant in contrast to the usual soft, friable and bleeding material found in malignant tissue. The recurrence should not rule out granuloma annulare. The biopsy report revealed the lesion to be granuloma annulare.

A CASE FOR DIAGNOSIS. Presented by DR. PHILLIPS.

J. D., a housewife, aged 35, presented a lesion on the left cheek, of eight years' duration. The lesion was circular and measured 1 inch (2.5 cm.) in diameter. The overlying skin was atrophic for its greater part and had a leathery sclerodermatous consistency. The margin was slightly elevated and indurated, and had a waxy ivory hue. Dotted throughout the lesion were a dozen or more small necrotic areas of the size of a match-head. The border of the lesion had extended slowly and was not painful. No response followed heavy roentgen-ray exposures.

DISCUSSION

DR. AMSHEL: I favored the diagnosis of lupus erythematosus, because of its chronicity, its location and the presence of adherent scales, patent follicular openings and atrophy.

DR. BUSMAN: The condition impressed me as being lupus vulgaris, because of the irregular border which is studded with active nodules. The scar shows nodules throughout, and it is difficult to see appreciable follicular dilatation.

The absence of lesions elsewhere is also against the diagnosis of lupus erythematosus of two years' standing.

DR. PHILLIPS: The diagnosis was not clear to me. I did not see any definite apple jelly nodules. I will attempt to obtain a biopsy and report at the next meeting.

A CASE FOR DIAGNOSIS. Presented by DR. PHILLIPS.

E. E. H., a man, aged 33, a pharmacist, had his first attack of the present eruption in June, 1925, and since that time has never been entirely free from the condition for longer than a few weeks at a time. The eruption has always been confined to the backs of the hands and fingers. It started as a vesicular eruption and rapidly became vesiculopustular. The lesions varied in size from that of a pin-head to that of a pea. Some of the lesions coalesced and formed large bullae undermining the skin. The individual lesions run a course of two weeks' duration and disappear, leaving a normal skin. Intense pruritus heralds the site of a lesion, but when the lesion appears the subjective symptom subsides. Repeated searches for fungi have revealed nothing. The past and present family history is negative.

DISCUSSION

DR. AMSHEL: This is a case of dermatitis venenata due to some drug used in the patient's occupation. I would advise that the patient be removed from his occupation for one month in order that his case may be studied further.

DR. BUSMAN: I believe we are dealing with an allergic reaction suddenly changed, and that the patient can develop such a skin reaction from chemicals which heretofore had no visible effect.

DR. HOLLANDER: The patient gave a history of using enamel or lacquer containing varnishes following which the eruption appeared. He favored the diagnosis of lacquer dermatitis.

DR. PHILLIPS: I have carefully checked the patient for all possible factors of plant, drug and external irritation, with no success. I shall try to carry out any suggestion offered and report the result later.

PELLAGRA (?). Presented by DR. PHILLIPS.

M. D., a girl, aged 6, presented a well defined, symmetrically placed dermatitis chiefly on the exposed parts of the body and occasionally on the buttocks and genitals. For the last five years the eruption has been recurrent and the longest period of freedom from attacks has been five weeks. Each attack was preceded by restlessness, nervousness and diarrhea. The eruption always appeared as an erythematous plaque, rapidly becoming bullous and terminating in desquamation within a week. During severe attacks, one or more finger and toe nails were shed. Stomatitis and denudation of the buccal and tongue epithelium were associated with the skin lesions. A marked photophobia accompanied each attack. The family history was negative. The diet had been chiefly bread, jelly and cereals, with large amounts of cake, sugar and cookies. An associated alopecia had been present since the onset of this disease.

DISCUSSION

DR. GUY: I feel that the cases exemplifies a congenital condition with glandular imbalance, in which the skin picture fits best a diagnosis of epidermolysis bullosa. I would call attention to the predominance of the

lesions on the points of irritation, their character and the recurrence of attacks, and the associated alopecia appearing at the age of 1 year is the same as in the cases reported by Kobner, Elliott and Wende as well as in the family group that I reported. In the latter group, occult blood as demonstrated in the stools during attacks and fluoroscopic examination with a bismuth meal suggested lesions of the intestinal mucosa. Perioral and perianal lesions were also present. During the interval between attacks irritation could not produce lesions, while during attacks lesions could be produced by friction. The older member of my group grew normal scalp hair at puberty, and the skin lesions had improved concurrently. The typical dermatitis on the areas exposed to sunlight with secondary atrophy was lacking in the case presented. The diarrhea was not diagnostic nor were the mucous membrane lesions, both appearing in epidermolysis bullosa as well as certain other conditions. Pellagra occurred in the spring and fall, and after a duration such as this case presented, mental symptoms and interference with reflexes were present. I think it is a simple case of epidermolysis, and that it will improve after puberty.

DR. BUSMAN: The definite history of bullae, the predominance of lesions over areas of trauma and irritation without pigmentation and thickening suggest the diagnosis of epidermolysis bullosa.

DR. NORRIS: I favor the diagnosis of epidermolysis bullosa because of the location of the lesions, the bullous aspect and the lack of mental symptoms.

DR. PHILLIPS: In the differential diagnosis, one has to consider the diagnosis of epidermolysis bullosa, but the fact that the lesions cannot be produced by trauma or irritation and appear on regions free from trauma, together with the periods of complete remission and the associated gastro-intestinal symptoms at the onset of the attacks, causes me to favor the diagnosis of pellagra.

GENERALIZED PRURITIS. Presented by DR. BEINHAUER.

D. G., a Jewish merchant, aged 54, married, presented a generalized erythematous eruption of six months' duration. The condition began in March, 1926, about the genitocrural regions. The first impression was one of a generalized eczema with a superimposed fungus infection of the feet and genitocrural regions. The patient was treated accordingly, and relief was given until four weeks ago, when an incessant pruritus developed, causing a marked loss in weight, general fatigue and loss of sleep which has resisted all forms of treatment. Examination revealed a short, stout patient much overweight and in apparent distress. The entire skin presented a diffuse erythema, covered with a generalized furfuraceous scaliness (which was negative for fungus) and with a tendency toward lichenification over the flexor aspects of the arms and legs. The skin was thickened and inelastic over its entire area. The results of the neurologic examination were negative. The liver was easily palpated, somewhat tender and rather resistant to the touch. The spleen was not palpated. A slight generalized adenitis was present. The mucous membranes were normal.

Examination of the blood revealed: red blood cells, 4,800,000; white blood cells, 6,000; hemoglobin, 90 per cent; the differential count was: 31 per cent lymphocytes, 2 per cent transitionals, 38 per cent polymorphocytes, 29 per cent eosinophils (varied to 49 per cent). The blood chemistry revealed: sugar 125 mg., uric acid 6.6 mg., urea nitrogen 27 mg. and creatinin 1.3 mg., per hundred cubic centimeters. The blood pressure was 128 systolic and 78 diastolic. The urine contained a faint trace of bile, a trace of albumin, no sugar, hyaline

and granular casts and red and white blood cells. The stool was pale yellow and of putty-like consistency, with no excess fat, no blood, no mucus and no parasites. The blood serum contained 2½ units of bilirubin (van den Bergh test), and gave a positive reaction to the Fouchet test, a negative reaction to the direct van den Bergh test and a positive (nonobstructive) reaction to the delayed van den Bergh test.

DISCUSSION

DR. HOLLANDER: It is unusual to find apparently normal laboratory observations in a patient who has a cyanotic appearance and whose condition apparently is serious. Exactly what the bilirubin content means I was unable to state, but it is worthy of further study, especially in cases of chronic pruritus.

DR. GUY: The facts that the patient is past middle life, is overweight and has an interstitial nephritis should be considered. This, plus the clinical picture of the liver disease was enough to produce the severe pruritus; the skin irritation was secondary to scratching.

DR. CRAWFORD: I believe the case is an unusual form of Dühring's disease.

DR. BEINHAUER: Although the patient did not complain of gastric or abdominal symptoms, there was no doubt of the tense firm liver border which was easily palpated and at times was tender to pressure. The chronic nephritis had a bearing on producing the pruritus, but I believe it was a secondary factor because the pruritus did not respond when treatment was directed toward the kidneys. I think that the patient is suffering from a progressive cirrhosis of the liver, and I will report the progress of the case at further meetings.

A CASE FOR DIAGNOSIS. Presented by DR. NORRIS.

R. C., a man, aged 66, born in Italy and for twenty-one years a resident of this country, married, presented a generalized eruption of months' duration. The past and family histories were negative. The patient said that he had been subject to "rheumatism" for the last seven years, during which recurrent attacks were frequent. Three months before presentation, he began to take a patent medicine for his joint pains without apparent relief. About one month ago, he noticed that a large, red, somewhat tender nodule had developed over the right shoulder area; since then the eruption had developed quickly, becoming generalized within the last two weeks.

Examination revealed a generalized nodular eruption, symmetrically placed and composed of large, rounded and flat, reddish-brown, nodular infiltrations, which remained discrete, spreading over the shoulders and down the mid anterior and posterior trunk, then outward over the hips, buttocks and thighs like a huge hour-glass. The facial expression was similar to that of a leper but lacked the nodular infiltrations of the eyebrow and ear regions. No ulnar nerve enlargement was present, and a generalized adenitis was lacking.

DISCUSSION

DR. PHILLIPS: The sudden onset speaks against a diagnosis of leprosy, leukemia and syphilis, and yet the picture could be labeled as any of these. I believe the case is one of a drug eruption, most likely caused by iodides, but any absolute diagnosis cannot be made without laboratory procedures.

DR. GUY: I agree with Dr. Phillips, and I think that the rapid involution of the lesions, the generalized eruption and the bright red color suggest a dermatitis medicamentosa.

DR. CRAWFORD: I am inclined toward the diagnosis of nodular leprosy. The interesting feature is the absolute symmetrical nodular infiltrations spread diffusely over the back, buttocks and thighs.

DR. NORRIS: The case offers possibilities of close differential diagnosis. The diagnosis of Hansen's disease first attracted my attention, but the sudden onset puzzled me. At the next meeting I will report the results of a complete investigation, especially from the standpoint of drug eruption, and I will have an analysis made of the internal medication which the patient has been taking.

Additional cases were reported as follows: Tertiary Syphilis by Drs. Hollander and Baer; Dermatitis Artefacta by Dr. Crawford; Staphyloma by Drs. Hollander and Fisher; Glossitis Areata Exfoliativa by Dr. Crawford; Dermatitis Medicamentosa by Drs. Hollander and Baer; Lupus Vulgaris by Drs. Guy and Jacob.

L. G. BEINHAUER, Secretary.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 26, 1926

H. H. WHITEHOUSE, M.D., *President*

MYCOSIS FUNGOIDES. Presented by DR. CLARK.

F. W., a housewife, aged 43, born in the United States, was first seen eight years previously with lupus erythematosus of the nose and cheeks. After four years of treatment with ultraviolet radiation and finally with solid carbon dioxide, the lesions were practically healed. Three years prior to presentation she began to suffer with severe itching of the back, followed a year later by eczema-like, pruritic lesions in that region, and later by lesions on the body, arms and face.

When presented, the patient had oval and round, fairly marginated, eczematous lesions with considerable infiltration. Between the lesions were groups of flesh-colored, pinhead-sized follicular nodules.

DISCUSSION

DR. MACKEE: I agree with the diagnosis and would like to call attention to the marked follicular element, which is not common in this disease. I have seen only two cases of this kind. When follicular lesions occur they usually do so in patches or groups. At first they consist of red follicular orifices which later become follicular papules. At times the papules coalesce and form plaques or tumors.

DR. WEIDMAN: Some of the papules were not inflammatory; i. e., they were visible before the inflammatory process started. It would seem that whatever the exciting cause might be it was primarily a simple hyperplastic one and that the inflammatory changes entered the picture only secondarly, albeit promptly. When the association with lupus erythematosus is pointed out, it makes one take notice on account of a certain similarity, viewed histologically, between lupus erythematosus and granuloma fungoides. Thus, what we have in both conditions is a stimulation of the reticulo-endothelial system, even though there are differences in the forms of the individual cells which are seen

in the two conditions. The question in this case is whether the same stimulus is operative in these two different parts of the body to produce the two different clinical disease entities. If so, the explanation might lie in the differing periods of life in which the stimulus occurred; the lupus erythematosus developed many years ago, whereas the granuloma fungoides was recent, and the difference in the disease expressions might be dependent on differences in the patient's metabolism at the different periods.

DR. FRASER: There are two interesting features in the case: first, the follicular type of lesions; second, the fact that itching was present for several years before the appearance of the eruption. Dr. MacKee said that it is difficult to make a diagnosis when only follicular lesions are present; it is still more difficult when only pruritus is present.

DR. HOWARD FOX: The clinical diagnosis of mycosis fungoides would appear to be reasonably certain from the appearance of sharply bordered patches, some of them showing a reticular tendency. The most diagnostic point is the difference in elevation of different lesions, some being slightly elevated and others markedly so. This, together with the itching, would indicate the presence of mycosis.

DR. WHITEHOUSE: Dr. Fox's diagnostic point in regard to the difference in levels is well taken.

DR. CLARK: Dr. MacKee brought out an interesting point in the examination. I remember seeing this patient with grouped, pruritic, tiny, follicular lesions on the back before any other lesions developed. Apparently these lesions developed into the typical mycosis lesions now present.

LUPUS ERYTHEMATOSUS TREATED WITH GOLD PROTEIN. Presented by DR. CLARK.

T. D., aged 25, from the Skin and Cancer Hospital, had had lesions of discoid lupus erythematosus on the face for at least five years. The lesions had resisted all recognized forms of treatment. Three months prior to presentation the patient began to receive intravenous injections of Schamberg's gold protein. In six weeks the lesions had almost disappeared. The reactions were so severe that gold thiosulphate was substituted for the protein and gold chloride was given by mouth. When presented there was but little evidence of the disease.

DISCUSSION

DR. MALONEY: I have had some experience with gold protein but not enough to reach any definite conclusions regarding it. I have not had any untoward reaction until today, when a case was reported to me in which six doses had been given at weekly intervals and a week ago enlarged glands had developed. I do not think the gold protein caused this condition, however. The result in Dr. Clark's case was good.

DR. FRASER: I treated one patient with gold protein. After twenty injections the lesions on the arms, hands and feet had completely disappeared, and those on the face were much paler. The patient was presented to the society, before and after treatment, at the January and April, 1926, meetings. Those members who had seen the patient at the January meeting commented on the marked improvement. I used one and a half ampules at each injection. There was no sign of reaction at any time. Although my experience is limited to one case, I feel that this gold compound will find a useful place in the treatment of lupus erythematosus.

DR. HOWARD FOX: The result in this case was excellent and encouraging. As a severe reaction was produced following the administration of a protein compound, why is it not possible that the beneficial results were due to a protein shock?

DR. CLARK: I have been interested in the treatment of these patients with gold protein, but have been rather disheartened by the magnitude of the reactions; some of the patients have been very sick—more than used to become ill after the administration of arsphenamine. I question whether it was not a protein shock that produced the marked effect in the lesions, as Dr. Fox has suggested; but Dr. Wright, Dr. Schamberg's assistant, assured me that they had had practically as good results with the gold thiosulphate as with gold protein. The latter has not given any unfavorable reaction up to the present, but it does appear to make the skin red and scaly at times. With the gold thiosulphate, I have also given gold chloride, 1/15 grain (0.004 Gm.) three times a day, in pill form, but the results have been less striking than with the gold protein. I have a private patient who has had severe lupus erythematosus for thirteen years. She has improved greatly under the gold treatment. She had unfavorable reactions from the gold protein, but not from the gold thiosulphate. It is necessary to discontinue the treatment when such a reaction occurs. This is the first method I have ever seen which apparently produced a direct influence on lupus erythematosus. Gold injections have not been very successful in the treatment of tuberculosis of the lungs. I have discussed this with Dr. Alexander Miller, as the treatment has been used at Saranac Lake. I have seen marked results from the use of gold thiosulphate injections in the treatment of necrotic granulomas.

DR. WISE: I should like to report briefly two cases. A man, aged 35, had extensive lupus erythematosus on the face and neck which cleared up under twelve treatments. However, there was a relapse a few days ago. The other case was that of a woman who during the treatment developed a partial opacity of both lenses. Dr. Schamberg said it had nothing to do with the treatment, and she was sent to an oculist, Dr. Wheeler; he also said it had nothing to do with the treatment. In her case the injections had not been beneficial to the lupus erythematosus.

DR. HIGHMAN: I know nothing about the gold preparations, but I have seen patients with lupus erythematosus improve no matter what treatment was administered and others that grew no better whatever was done. I should like to know whether those who have employed the gold treatment have compared their results with those in cases in which other forms of treatment have been given. The treatment should be controlled.

LUPUS ERYTHEMATOSUS DISSEMINATUS TREATED WITH GOLD PROTEIN. Presented by DR. BECHET.

J. K., aged 54, from Dr. Atkins' service, was first presented before the Atlantic Dermatological Conference, Dec. 16, 1926, and the case was reported in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**13**:701 [May] 1926). When previously presented, he had large scaly typical plaques of lupus erythematosus over most of the face, neck, chest, arms and hands. His general health was poor and there had been rapid loss of weight. While the physical examination of the lungs was negative, a roentgen-ray examination showed a bilateral peribronchial thickening.

After only seven or eight injections, the disease had entirely disappeared from the arms and trunk, leaving only a few scattered discoid lesions on the

face. The patient's general condition improved rapidly; within a few weeks he gained more than 18 pounds (8 Kg.). The drug was discontinued in March, and from that time on there had been no recurrence of the disseminate lesions, but there were still some discoid lesions on the face.

DR. MACKEE: I used the gold protein in three cases. One patient was a man with a marked discoid lupus erythematosus of the face and neck which did not show improvement until the eighteenth injection, and then cleared up entirely. Later he had a slight recurrence and was given gold thiosulphate. The condition is again improving. The other patients were young women who had the disseminate type, severe cases. After six or eight injections of gold protein there was no improvement. Sudden violent reactions then occurred —chills, fever and prostration. They were very ill for several weeks. During this reaction there was a generalized eruption suggestive of dermatitis exfoliativa. They recovered from the reactions, and the condition was improved slightly.

DR. WHITEHOUSE: Dr. Fox's suggestion as to whether the reaction is from the protein or the gold is interesting and should be investigated. Dr. Schamberg seemed to think it was from the protein. It may be that Dr. Highman's question has been answered by what Dr. Bechet has said. Dr. Schamberg reported two cases in which the patients had derived no benefit during thirty years from various methods of treatment. With the employment of gold protein therapy the condition cleared up materially, and the patients themselves were enthusiastic about this treatment.

LUPUS VULGARIS DISSEMINATUS. Presented by DR. LANE.

I. S., a salesman, aged 23, presented fifteen lesions on various parts of the body; there were several on the face and one on the left sole. They varied in size from that of a dime to about 3 inches (7.6 cm.) in the longest dimension. They began to appear at about the age of 2 years. There had not been any ulceration. The lesions were dull red, considerably elevated, slightly scaly and marginated, and showed large apple-jelly nodules.

DISCUSSION

DR. MALONEY: I believe that the lesion on the chest confirms the diagnosis of lupus vulgaris. The lesions on the arms suggest psoriasis, but they are undoubtedly all lesions of lupus vulgaris.

DR. HIGHMAN: I wish the members of the society would reflect on the subject for a year and then have a symposium concerning the basis on which lupus vulgaris should be differentiated from skin tuberculosis.

DR. WEIDMAN: One of the lymph nodes back of the tumid ear was enlarged, yet in spite of the large plaques over the elbows, the epitrochlears were not. This illustrates the capriciousness of skin tuberculosis in the way of deep extension.

DR. MACKEE: I usually treat such patients with the roentgen ray and tuberculin. Patches of large, elevated, active nodules are often amenable to irradiation. The atrophic type with deeply embedded nodules does not respond well to the roentgen ray or radium treatment. In my hands tuberculin therapy has been successful in the nonulcerated cases if the first dose is exceedingly small and the treatment is continued for a year or two with gradually increasing dosage.

DR. LANE: The man had been treated by irradiation, without benefit, before he came to me, so I did not try it. He said that the glands had been enlarged for a long time.

PARAPSORIASIS EN PLAQUES. Presented by DR. WISE.

M. S., a man of Russian birth, aged 65, presented lesions of about seven months' duration, consisting of oval and roundish, well defined but not sharply marginated macules on the chest, back and thighs, light pink, from ½ to 1 inch (1.2 to 2.5 cm.) in the long dimension, free from scales and without infiltration. There was slight itching, but the subjective symptoms were trivial. On the back they were arranged to some extent like those of pityriasis rosea, in the lines of cleavage, and the entire eruption simulated that disease. However, the lesions had remained unchanged for seven months, there was no scaling and no history of a herald patch, nor was there any wrinkling of the skin in the patches. Roentgen-ray and ultraviolet light treatment proved unavailing. The history as to the ingestion of drugs was negative.

DISCUSSION

DR. MALONEY: The eruption seems to lack the scaliness of a parapsoriasis and it seemed to follow the arrangement of a pityriasis rosea; it may be due to some toxic condition — a persistent toxic dermatitis.

DR. MACKEE: I cannot agree with the diagnosis of a toxic dermatitis. It would be most unusual for a toxic dermatitis to last so long, especially with such fixed lesions. Drug eruption and atypical prefungoid mycosis fungoids should be considered. My tentative diagnosis is parapsoriasis. The fact that the roentgen-ray treatment was not efficacious is against the diagnosis of mycosis fungoides.

DR. WISE: Replying to Dr. Maloney's remark, the scaling is absent because the man bathes twice a day and uses an ointment freely. As to the pityriasis rosea, he received eight exposures to the roentgen ray without any visible effect on the condition.

A CASE FOR DIAGNOSIS — PEMPHIGOID ERUPTION. Presented by DR. HOWARD FOX.

M. H., a boy, aged 4 years, born in the United States, of Jewish parents, had suffered from an eruption for nine months. It followed an attack of measles. The case was presented last month at the Dermatological Section of the New York Academy of Medicine as a case of impetigo. He now presented a pemphigoid eruption consisting of diffuse, reddish, infiltrated, fairly well defined areas, especially marked on the abdomen and groins. The surface of the patches showed numerous collapsed vesicles and bullae, and frequently at the borders of the patches individual tense bullae were seen arising from normal skin. Nikolsky's sign was absent. A month previously the eruption presented a somewhat different appearance. There was marked itching shown objectively by excoriations and by constant scratching. The itching had lessened greatly. Several vesicular lesions had been present on the tongue. the child was well nourished, of blond type and in fair general condition.

DISCUSSION

DR. SCHWARTZ: The condition seemed to me to be an extensive case of bullous impetigo contagiosa. We have seen a number of such cases at the Lying-in Hospital, and the general distribution, etc., certainly closely resembled that in this case. I think it is a staphylococcic infection.

DR. HIGHMAN: It is either a pemphigus or dermatitis herpetiformis. Another possible hypothesis is pyoderma. The intractability should be considered against a diagnosis of impetigo. The child has had a lesion on the tongue and lesions all over the body and thighs, and the lesions on the other part of the body lead me to believe that it is a case of pemphigus.

DR. WEIDMAN: I cannot come to any conclusion in regard to the bullous phase of the eruption, but its diffusion and its distribution in the inguinal regions makes me think of a yeast infection — at any rate, a dermatomycosis. Possibly there may be two conditions present — a pemphigus or a pemphigoid condition, complicated by the presence of a secondary yeast infection.

DR. WISE: I think it is a pemphigoid condition but not a true pemphigus. I saw the patient some months ago, and at that time he had pemphigoid lesions. I do not subscribe to the diagnosis of dermatitis herpetiformis.

DR. MACKEE: I think the case is one of a staphylogenic eruption. In order to have a diagnosis of pemphigus, bullae must develop on unaltered skin. This did not occur in the case presented.

DR. LANE: My impression was the same as that of Dr. Schwartz. Dr. Weidman's suggestion had not occurred to me. The location is favorable for pyoderma as well as pemphigus. It is worse around the groins and lower part of the abdomen, and the child has not yet reached the age when he has complete control of urination; these locations are constantly damp.

DR. WHITEHOUSE: I am inclined to consider the condition a simple streptococcic infection. The boy had been sick with influenza and diphtheria previous to this attack, and the condition of the skin followed. Dr. MacKee's suggestion of red patches preceding the lesions is most important. I would not consider pemphigus. I think the condition is a pyodermic dermatitis. Someone suggested impetigo herpetiformis; I do not think it is that. Almost all cases occur in pregnant women, and the lesion in impetigo herpetiformis is primarily a pustule and always a pustule. I never saw a bulla or a vesicle, and that is one of the cardinal observations in impetigo herpetiformis. In my case, the patient was a man.

DR. HIGHMAN: I did not notice the history of diphtheria, and think that the Klebs-Loeffler bacillus should be sought.

DR. HOWARD FOX: I am pleased to have had this long discussion, though I am more confused than ever as to the diagnosis. When the patient returns I will make some bacteriologic examinations, following the suggestions made by Dr. Weidman and others.

ACRODERMATITIS CHRONICA ATROPHICANS WITH HEALED SQUAMOUS CELL EPITHELIOMA. Presented by DR. WISE.

Mrs. G. B., aged 46, presented atrophy of the extremities, extending from the wrists to the shoulders and from the bases of the toes to the groins and up to the level of the umbilicus. The skin had the appearance associated with acrodermatitis atrophicans. The duration was about thirty years. Apparently the general health of the patient was unaffected. Many portions of the skin had become eczematous, especially that of the abdomen and lower portion of the back and the buttocks. Midway between the knee and groin, on the inner aspect of the right thigh, was an elongated scar, four inches by one-half inch (10 by 1.2 cm.) in dimension, which was the site of an epithelioma developing within the atrophic skin. When the patient first came under observation, this area exhibited a round ulcer, about 6 inches (15 cm.) in diameter, with

crateriform edges, the base of the ulcer having a granulomatous sloughing surface. Six months prior to presentation, the patient was advised to enter the Memorial Hospital, where she was under the care of Dr. Quick, whose treatment brought about the excellent result shown.

LICHEN PLANUS WITH PECULIAR SERPIGINOUS LESION ON RIGHT KNEE. Presented by DR. BECHET.

Y. P., a girl, aged 16, said that she first noted an eruption on the right knee, and a few months later a generalized eruption appeared, particularly noticeable on the arms. On inspection, a large number of characteristic shiny violaceous umbilicated papules were seen on the arms; on the right knee was a purplish serpiginous patch; it was not raised or infiltrated, and the color could be pressed out only with difficulty. It did not itch, and bore a slight resemblance to an angioma. It was certainly an atypical form of lichen planus, and the patient was presented for that reason.

DISCUSSION

DR. HOWARD FOX: I think the entire eruption is unquestionably lichen planus, the lesions on the arms and legs being characteristic. The interesting feature of the case was the reticulated pigmentation, which is not so extraordinary considering the fact that the disease at times assumes a somewhat reticulated appearance.

SEBORRHEIC DERMATITIS OF THE SCALP WITH HYPERKERATOTIC LESIONS ON THE CHEST AND UPPER PART OF THE BACK. Presented by DR. BECHET.

E. J., a girl, aged 12, came to Dr. Aitken's service with her mother, who said that three months previously she had noticed an excessive oily scaly condition on the scalp. The child presented for examination an excessively dry condition of the hair and scaliness of the scalp. There were also innumerable minute hyperkeratotic lesions over the sternal region and in the middle of the upper part of the back, in the so-called seborrheic locations. Many of these follicular keratotic lesions were horny, much like lichen spinulosus. The skin of the rest of the body was normal.

DISCUSSION

DR. HOWARD FOX: I do not think this condition is a seborrheic dermatitis, as I did not see any signs of inflammation. There was some redness where the skin had been rubbed during examination. All that was seen was an eruption of follicular plugs, with some grouping and a slight tendency to form spinous prolongations. I would call the lesion a circumscribed keratosis pilaris, or possibly a lichen spinulosus of a mild type.

DR. WILLIAMS: I wish that some one with a ready pen and genius for classification would prepare a good definition of seborrheic dermatitis. We all recognize a type of disease occurring on the scalp, on the presternal region, and in the middle of the back, which is characterized by a dull red, slightly elevated border, the redness sometimes covering the whole patch but usually showing a tendency to clear in the center. There is always some greasy scaling, often most marked at the periphery. This disease may well be described as seborrheic dermatitis. At any rate, it is a dermatitis, it appears in the regions in which sebaceous glands are frequent and large, and it is greasy. The greasiness may be due to increased secretion of sebaceous matter or to bacterial

growth in the scales, or perhaps to some other cause, but the origin of the greasiness is not important for the present discussion.

This child does not show any dermatitis or greasiness, and the disease is not confined to the seborrheal regions. In fact, the condition is generalized and the skin everywhere is abnormally dry. Whatever condition the child has, I do not see how it can be true seborrheic dermatitis. It is true that the name seborrheic sicca has been applied to dry dandruff of whatever cause, and this use of a term has been responsible for as much loose thinking and speaking as any other mistake in dermatology. This has caused many physicians who should know better to call every case of dandruff, and almost every case of scaling, wherever found, seborrheic dermatitis.

The present case I would interpret in a different manner. As noted above, the skin everywhere is abnormally dry, and this dryness includes the scalp as well as other parts of the body. Occurring on the scalp, it has produced a dry furfuraceous scaling, which is not related to any form of infection. The hair is dry and lusterless; the skin is dry everywhere, and the pilosebaceous follicles are enlarged and horny. The involvement of the follicles varies in different parts of the body, and on the anterior part of the chest it has produced fine spines projecting from the small horny caps. Dermatologists may call the condition lichen spinulosus if they wish, but giving it a name does not really increase the knowledge of the condition.

In addition to these abnormalities in the skin, the child is obese and has a narrow palatal arch. The whole picture is that of a developmental disorder, which is most likely due to maladjustment of endocrine function, and I believe that in this case the pituitary gland is the gland most at fault.

This disorder often disappears at puberty.

DR. HIGHMAN: I agree with Dr. Williams completely in what he said about seborrheic dermatitis; the name is one of the absurdities that has been allowed to creep into the vocabulary. I can only express my unqualified approbation of what he said. I think the child has a dyscrasia of the type that Dr. Williams pointed out — clinically, lichen spinulosus and keratosis suprafollicularis on the elbows, complicated by ordinary dandruff.

DR. MACKEE: I cannot agree with the diagnosis of seborrheic dermatitis. I consider the case one of more or less generalized xeroderma or very mild ichthyosis, with allied conditions such as keratosis pilaris. I think that the scalp condition is one of xeroderma capitis and not seborrhea. In using the word seborrhea in connection with the scalp, I mean of course the seborrhea sicca of the German school or pityriasis simplex capitis of the French school. This condition progresses into steatoid pityriasis, and finally into oily seborrhea.

DR. WILLIAMS: The condition of the scalp is probably part of the general condition. I do not think it should be called seborrhea in any case. The child has scales, but the condition is not seborrhea. I will go even further: many cases that are classified as seborrhea sicca are cases of exactly this type, showing only that symptom and not the others. They are going through phases of development and the glands are not properly coordinated, and when the development ceases the conditions disappear. All cases do not go through the three stages mentioned by Dr. MacKee.

DR. WHITEHOUSE: I regard the condition not as seborrhea but as a defect of the skin due to faulty action of its glandular elements.

DR. BECHET: I agree with the remarks made, with the exception of the suggestion of xeroderma. The parents of the child are sure that three months

previously the skin was absolutely normal. The skin is normal, soft and not dry with the exception of that on the scalp, chest and upper part of the back. I think that Dr. Williams' remarks are pertinent; the child is undoubtedly suffering from some hypofunction of one or a group of the endocrine glands — probably the pituitary — and the entire dermatosis is due to this dysfunction.

BROMIDE ERUPTION. Presented by DR. SCHWARTZ.

N. A., a man, aged 51, gave a history of an eruption appearing shortly after a slight injury to the skin, four months previously. The lesion, located over the anterior middle third of the right leg, consisted of an erythematopapillomatous area several inches in diameter, which presented numerous points of pustulation. A piece of tissue taken from the edge of the lesion was examined microscopically and showed the presence of a plug in a follicular opening, with some central necrosis, hyperplasia of the epiderm and extensive irregular downgrowth of epithelial pegs. In one area there was a localized outgrowth of papillae. In the corium were numerous groups of dilated lymph and blood vessels with thick walls. There were moderate round cell infiltration and marked diffuse fibrosis. The histologic picture was that of a chronic inflammatory process, not pointing definitely to any specific picture. Tuberculosis verrucosa cutis, blastomycosis and syphilis were excluded.

The patient denied syphilis, and the Wassermann reaction was negative. A history of drug ingestion could not be obtained, but the diagnosis of bromide eruption seemed the most likely.

DISCUSSION

DR. MACKEE: I cannot make a clinical diagnosis. Clinically the lesion may be bromoderma, iododerma, blastomycosis or tuberculosis verrucosa cutis. The possibility of a drug eruption must be excluded carefully by interrogation and by laboratory work. Blastomycosis must be excluded by repeated microscopic examinations. Tuberculosis can probably be excluded by the rapid evolution, which is also rather rapid for blastomycosis.

DR. WEIDMAN: Does any one know of a simple clinical test for small quantities of bromides? Bromine can be distinguished readily enough if there are large quantities. In these debatable eruptions, dermatologists commonly overlook the necessity for making a urinalysis.

DR. WISE: I am in favor of the diagnosis of blastomycosis. I thought Dr. Wile had published a relatively simple test for bromine in one of his articles on the subject.

DR. WILLIAMS: As to a differential diagnoses between bromoderma and blastomycosis: Against the diagnoses of bromoderma is the fact that there is no history of drug ingestion, but the lack of history is a fairly common occurrence. Against the diagnosis of blastomycosis is the short duration; four months is too rapid a development for blastomycosis of that kind. Nevertheless, I incline to that diagnosis, and I hope further laboratory examinations will be made.

DR. HOWARD FOX: Granulomatous lesions like this might be due to the ingestion of either bromides or iodides, though they would be more likely to follow the use of bromides. In obtaining a history of drug eruptions it is often difficult to make the patient realize that patent remedies for headaches, and "blood remedies," may be at fault. This was true in the case of severe bromoderma following the use of Bromo-Seltzer reported by Waugh, and in a similar case of mine shown before this society.

DR. WHITEHOUSE: I was wondering whether the therapeutic test of sodium chloride intravenously would help in this diagnosis. I interrogated the patient as to whether he had had headaches. He denied ever having had any, and was not, therefore, a probable consumer of Bromo-Seltzer.

DR. FRASER: My first thought was that this was a bromide or iodide eruption. Blastomycosis was also considered. Further laboratory tests will be made with the view of settling the question of diagnosis.

DR. SCHWARTZ: It was thought, by exclusion, that in spite of the negative history the most likely diagnosis was bromoderma. As a rule, these histories are not to be relied on. I propose to give the patient intravenous injections of physiologic sodium chloride solution and to test the urine for the presence of bromine subsequently.

CHRONIC PURPURA (?). Presented by DR. FRASER.

F. J. H., aged 61, presented purpuric lesions varying in size from that of a pinpoint to that of pinhead, with a duration of between seven and eight months. They first appeared on the legs and thighs. There was no history of any infection. The patient was presented in order to get an expression of opinion from the members as to the cause of the hemorrhage.

DISCUSSION

DR. MACKEE: I think that the case is one of simple purpura due, perhaps, to a combination of causes. It may be partly traumatic, partly hemostatic and partly toxic. Support for the local circulation and investigation of the patient's general health are indicated.

DR. WILLIAMS: I agree with Dr. MacKee.

DR. WISE: The lesion is probably a hemostatic condition of the skin, aggravated by indigestion and pruritus. This condition was described by Dr. Klotz about thirty years ago under the term dermatitis hemostatica. I believe that the patient is neurotic and apprehensive and that the treatment should include psychic therapy, to distract his mind from the skin condition.

DR. WHITEHOUSE: I agree with what Dr. MacKee said. The man is of middle age, intelligent and interested in his condition. I think that all the lesions can be accounted for on the basis of a toxic rash emanating from the intestinal tract.

PEMPHIGUS. Presented by DR. BECHET.

A man, aged 52, had been presented three years previously with the same diagnosis. At that time the lesions were confined entirely to a patch about 3 inches (7.6 cm.) in diameter on the chest and in the middle of the back between the scapulae. There were also a few lesions in the mouth. The diagnosis was accepted.

Since that time, the patient had been under constant observation, without any extension of the disease until two or three weeks previously when there was an extensive outbreak of bullae over the trunk, legs and arms; many of the bullae arose from apparently healthy skin. Nikolsky's sign was present, and the lesions seemed to be extending rapidly.

The patient was presented in order to demonstrate the fact that occasionally pemphigus runs a comparatively benign course for a number of years and

then suddenly becomes markedly aggravated, usually terminating in death within a few months. The presenter had in mind two cases of pemphigus with the lesions limited to two or three bullae in the mouth for two or three years, and then a sudden outbreak of bullae over the body, followed by death in a few months.

DISCUSSION

DR. MACKEE: I think the condition is an aberrant type of dermatitis herpetiformis. The lesions show the usual predilection for the buttocks and upper part of the back. Herpetiform grouping and severe itching are present. The lesions are papular as well as vesicular. Lesions of the mouth are occasionally seen in Duhring's disease. The entire picture suggests dermatitis herpetiformis more than any other disease.

DR. WEIDMAN: It seems to be a borderline case, in the same way that pemphigus circinatus has for a long time been regarded at one time as Duhring's disease and then as pemphigus.

DR. WISE: I incline to the diagnosis of pemphigus, and I think a few cases of this kind are amenable to cure with large doses of arsenic. I use a 2 per cent solution of arsenious acid, by subcutaneous injection.

DR. WILLIAMS: The grouping, the pruritus, the occurrence of erythematous lesions as well as bullae, all favor a diagnosis of dermatitis herpetiformis at present. However, I agree that these cases are confusing and that it is not safe to make a positive diagnosis until the patient is dead.

DR. MALONEY: I favor the diagnosis of dermatitis herpetiformis on account of the character of the lesions, the tendency to grouping and the itching.

DR. HOWARD FOX: I think it is an atypical case of Duhring's disease rather than of pemphigus, because the lesions show the classic symptoms of polymorphism, grouping, itching and the tendency to recurrence.

DR. BECHET: I have observed this patient for three years and have seen recurring bullae in exactly the same locations — the sternal region, between the scapulae and in the mouth — and nowhere else during that period. The lesions are invariably bullous, and all of them are in the same stage of evolution; some of them arise from apparently healthy skin. Nikolsky's sign can be demonstrated. There is some itching, but its presence does not exclude pemphigus. Stelwagon states that it can be present, and he classifies such cases as pemphigus pruriginosus. On the other hand, I have never seen dermatitis herpetiformis occur in exactly the same location for three or four years and consist entirely of successive crops of bullous lesions alone. Pigmentation is also absent and the itching is not severe, as evidenced by the lack of definite scratch marks. The fulminant acute outbreak after years of quiescence is also against the diagnosis of dermatitis herpetiformis and in favor of that of pemphigus.

ALOPECIA GENERALISATA IN A SYPHILITIC NEGRO. Presented by DR. WISE.

D. A., a colored man (mulatto), aged 34, married, born in the West Indies, who had had two healthy children, his wife having had no miscarriages, presented a complete alopecia areata of the scalp and a nudation of the outer portion of both eyebrows and of the axillary and pubic regions. The history was that he had had a chancre two years after the first appearance of the alopecia, the latter beginning about ten years before examination; that is,

the chancre was said to have appeared after the alopecia. Despite this fact, he received about fifty injections of arsphenamine and twenty-five of mercury on the supposition that the loss of hair might be due to the syphilitic infection. Five years before, he developed a gumma of the testis, which responded readily to antisyphilitic remedies. During the entire progress of both diseases the Wassermann reactions — twelve within five years — were always negative. The alopecia was said to have become worse following the antisyphilitic treatment. His wife's blood reaction was negative, and the health of his two children was said to be normal. The patient was presented with the idea of correlating the alopecia areata with the syphilitic infection.

DISCUSSION

It was agreed that the alopecia was independent of syphilis.

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